EXHIBIT C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 4 Cases*	

GENERAL EXPERT REPORT OF STANLEY ZASLAU, MD, MBA, FACS

Regarding Gynemesh PS and Prolift

This report summarizes my qualifications, training and experience, and my general and my opinions about Gynemesh PS and Prolift. My opinions are based on the information I have reviewed as of the date of this report. If I receive additional information before trial, I may form additional or modified opinions. All of my opinions are expressed to a reasonable degree of medical and scientific certainty or probability and are based on my education, training, experience, professional society guidelines, analyses, position statements, medical literature, the IFUs and Patient Brochures, Professional Education materials, deposition testimony, and other materials I have reviewed, as summarized in the attached reliance list. I have also reviewed the Expert

Reports submitted by plaintiffs' experts as well as the documents and literature cited in the body of their general reports. Exhibits that may be used to illustrate and support my findings are referenced herein and/or included in the literature and documents from my attached reliance list.

I. Background, Training and Experience

I received my undergraduate degree in biology and psychology from Boston University in 1988. I attended Hahnemann University School of Medicine and received my MD degree in 1994. I completed my internship in general surgery and urology residency training at Mount Sinai Medical Center (New York) in 2000. I completed an additional year of training as part of the Consortium Group Urologic Surgical Associates in Brooklyn, New York, where I received advanced training in incontinence, voiding dysfunction, prosthetics and pelvic prolapse.

Upon completion of training in 2001, I accepted a position as Assistant Professor of Urology at West Virginia University. My practice area of focus was incontinence and voiding dysfunction. I achieved urology board certification in urology in 2003. I was promoted to Urology Residency Program Director and Associate Professor of Urology in 2005. I was promoted to Professor and Chief of the Division of Urology in 2010.

In 2013, I took and passed the inaugural subspecialty certification examination in Female Pelvic Medicine and Reconstructive Surgery and was the first such certified professional in the State of West Virginia. In 2013, I was named as the Associate Chairman of Education and Research for the Department of Surgery. My

practice is still very active in incontinence, voiding dysfunction and sexual dysfunction in men and women. I serve as the Co-Director of the West Virginia University Center for Voiding and Sexual Dysfunction. I have been involved in teaching urology and urogynecology to medical students, residents and fellows. This instruction includes the basic surgical risks that are associated with both mesh and non-mesh pelvic floor repair and incontinence surgeries. Knowledge of these universal risks of both mesh and non-mesh pelvic floor repairs, such as failure/recurrence, pelvic pain (transient or chronic), dyspareunia (transient or chronic), etc., are commonly known risks that residents, fellows, and pelvic floor surgeons would be expected to know through their education, training, review of medical textbooks and literature, and are tested on during in-training and board-certification examinations.

I am very active in the practice of incontinence, voiding dysfunction and pelvic floor prolapse. I learned to perform the Prolift procedure in practice beginning in 2004 and was able to appreciate the ease of performing this procedure. I was also taught how to perform pubovaginal slings and came to appreciate the added morbidity associated with the abdominal approach to harvest fascia for these cases. Vaginal wall suspensions were also commonly performed during that time and their failure rates and complications of suture erosion and extrusion were also well known.

During my year of advanced training, I assisted with and performed many prolapse procedures without any intraoperative complications and with excellent post-operative results. From 2001 until 2012, I performed over 100 Prolift procedures. This would include a combination of Prolift Anterior, Posterior and Total procedures. I am also comfortable and routinely perform plication based repairs with and without fascial

interposition as indicated or as desired by patients. I was able to appreciate the ease of performing the procedure and the satisfactory short-term and longer-term results. I have never had a significant bladder or rectal injury. With all procedures I perform I carefully review with patients preoperatively, postoperatively and at each subsequent office visit the commonly known risks and potential complications of pelvic floor surgery including incontinence, recurrence, voiding dysfunction, pain, sexual dysfunction, mesh erosion and extrusion. As part of my counseling process with patients I discuss my complication rates, which are generally consistent with the published rates in the medical literature. This has resulted in excellent long term patient satisfaction over 15 years.

A copy of my C.V., which sets out my training, education and experience and my publications, is attached as Exhibit A. I am being compensated for my work in this matter at a rate of $500 an hour. For work required to be turned around in 10 days or less, my rate increases to $750 an hour. Depositions and appearances at trial follow a different fee schedule. I have given depositions and testified at trial as an expert witness within the past four years in a number of cases. Please see listing attached as Exhibit B.. Additionally, my reliance list is attached as Exhibit C.

II. Introduction to Normal Pelvic Anatomy and Pelvic Organ Prolapse

In normal patients, with normal muscle, connective tissue (fascia) and neural tone, the upper vagina will lie nearly horizontal when the female body is upright. This is because the levator ani muscle with its normal structure and strength and the vagina with its adequate depth. A “flap valve” is created in which the upper vagina presses against

the levator plate when there is an increase in intra-abdominal pressure. This describes normal pelvic floor support.

In patients with pelvic organ prolapse (POP), dysfunction of this delicate balance between muscle tone, fascial support and neural function is impaired. The result is herniation as in other parts of the body such as the inguinal canal or the abdominal wall. The etiology of pelvic organ prolapse is multi-factorial. In some patients, there is a loss of the support maintained by a complex interaction among various tissues and muscles. These can include the levator ani, the vagina, and the connective tissue. Dysfunction of any or all of these entities can lead to pelvic organ prolapse. For example: neurologic injury from stretching of the pudendal nerves may occur during childbirth. Additionally, when the levator ani loses its muscle tone, it moves from a horizontal to a semi-vertical position, creating a widened genital hiatus leading to pelvic organ prolapse. Connective tissue support can also fail possibly as a result of decreased collagen integrity and tearing which can lead to prolapse. Risk factors for prolapse are well described in the literature and can include factors such as: ethnicity, advanced age, increasing BMI, menopause, low socioeconomic status, increased intra-abdominal pressure, chronic cough caused by smoking, chronic lung disease, straining with chronic constipation or repeated heavy lifting, current pregnancy, previous prolonged labor, instrumental delivery, episiotomy, increasing parity, weight of babies, previous surgery such as hysterectomy and previous prolapse surgery.

Awaad (2012) performed a community-based study on the incidence and risk factors for POP. They noted that 251 (49.8%) women had clinically significant POP in their study. When stratified by life decade, POP prevalence was 20.4% for women aged

20 to 29 years, 50.3% for women aged 30 to 39 years, 77.2% for women aged 40 to 49 years, and 74.6% for women aged 50 to 59 years, suggesting a plateau in prevalence in the decade after menopause. They also noted clinically significant POP found in 3.6% of nulliparous, 6.5% of primiparous, 22.7% of secondiparous, 32.9% of triparous, and 46.8% of tetraparous women. Further, increasing age, increasing vaginal parity, and a body mass index higher than 24 kg/m were found to be significant risk factors for POP. Finally, the authors noted that combined clinical symptoms of pelvic heaviness, urinary disturbances, and a feeling of bulge in the vagina were predictive of POP.

It is known that POP can negatively affect quality of life. This leads to discomfort and patients will avoid sexual relations. Many patients with significant POP have pain because the prolapse is difficult to reduce, interferes with sexual intercourse or other such activities. For these reasons is it is appropriate to perform surgery to treat such prolapse.. This POP can lead to significant embarrassment, depression and social isolation. These problems can also lead to sleep deprivation and other associated conditions.

Ghetti (2010) compared depressive symptoms in women with and without prolapse and evaluated impact on quality of life. In this secondary analysis of a case-control study assessing the effect of prolapse on body image, patients had prolapse and sought surgery for symptoms (POPQ stage > or = 2). They found that patients with POP were 5-fold more likely than controls to have depressive symptoms. Patients with depressive symptoms had higher PFIQ scores than patients without symptoms. PHQ-9 scores improved post-operatively. They concluded that depressive symptoms are

common in women with prolapse and a decrease in those symptoms occurred following surgical treatment.

Jha (2016) sought to compare the effect of POP and SUI on the sexual function of women undergoing surgery for these conditions. They evaluated 343 women undergoing surgery for either SUI or POP. While the overall impact of POP and SUI was not significantly different in the two subgroups ($p = 0.703$), both patients (73% vs 36%; $p = 0.00$) and partners (50% vs 24%; $p = 0.00$) avoid intercourse significantly more frequently in cases with POP compared with SUI. They concluded that the impact of bothersome SUI or POP on sexual function was found to be similar, but patient and partner avoidance of sexual relations in women with POP was greater than those with SUI.

Ghetti (2015) studied the emotional burden experienced by women seeking treatment for prolapse to determine the impact on women's emotional well-being. 44 women participated (25 in focus groups and 19 in phone interviews). The authors in their analysis revealed the following 3 main themes: (1) emotions associated with the condition of prolapse (minimal emotions, annoyance, irritation, frustration, anger, sadness, anxiety, depression), (2) communicating emotions related to prolapse (to friends, family, healthcare providers), and (3) emotions relating to treatment (both positive and negative effects). They concluded that prolapse significantly impacts women's emotional health and subjective well-being.

Ghetti (2015) believed that sleep disturbance in women seeking treatment for pelvic organ prolapse (POP) existed and studied this using a validated sleep scale. 407 women were enrolled. They found that women with poor sleep quality were younger,

had more medical comorbidities, more pelvic floor symptoms, more nocturia, more depressive symptoms, and took more time to fall asleep. Worse sleep scores were associated with each of the PFDI subscores (urinary, prolapse, bowel), depressive symptoms, severe nocturia symptoms, and number of comorbidities. They concluded that poor sleep is prevalent in women with prolapse. Further, pelvic floor symptoms as measured by PFDI sub-scales, were associated with poor sleep quality.

III. Anatomical features of POP

The maintenance of continence and prevention of POP rely on the support mechanisms of the pelvic floor. The bony pelvis consists of the hip bones, which are fused to the sacrum posteriorly and to each other anteriorly at the pubic symphysis. Muscle support within the pelvis is derived from the levator ani and coccygeus muscles. These muscles are are attached to the inner surface of the minor pelvis and form the muscular floor of the pelvis. In addition, the urogenital diaphragm, is present over the anterior pelvic outlet below the pelvic diaphragm. The perineal body is a pyramidal fibromuscular structure in the midline between the anus and vagina with the rectovaginal septum at its cephalad apex. This is an important confluence of muscles and fascia that provide support for the posterior pelvic floor. The bladder, urethra, vagina and uterus are attached to the pelvic walls by a condensation of connective tissue known as the endopelvic fascia. This structure lies immediately beneath the peritoneum and is a continuous unit. There are various thickenings (condensations) in specific areas within the pelvis. The connective tissue supports of the urethra, bladder, and vagina extend to the arcus tendineus of the pelvic fascia on the pelvic diaphragm. There is a “hammock”

of anterior vaginal wall tissue, bridging the gap medially in the urogenital hiatus that supports the bladder neck and urethra.

The pubourethral ligaments extend from the urethra to the pubic bone. These important ligaments provide support for the urethra and keep the bladder neck closed at rest. The uterosacral ligaments are attached to the cervix and upper vaginal fornices posterolaterally. Posteriorly, they attach to the pre-sacral fascia in front of the sacroiliac joint. The connective tissue of the uterosacral ligaments is continuous with that of the cardinal ligaments around the cervix. The cardinal and uterosacral ligaments hold the uterus and upper vagina in their proper place over the levator plate. The posterior vaginal wall, below the cardinal ligaments, is supported from the sides by the paracolpium, which is attached to the rectovaginal fascia and pelvic diaphragm. The anterior and posterior fascial layers unite along the sides of the vagina. The rectovaginal fascia is found mostly at the sides and is extremely thin in the midline of the vaginal wall. However, a posterior rectovaginal septum, consisting of fibromuscular elastic tissue, extending from the peritoneal reflection to the perineal body contributes to the anatomy of this region.

IV. Staging of POP

The severity of prolapse is graded with The Baden–Walker Halfway Scoring System. The assignment of a score to each of six specific midline sites encodes a large amount of information in a small amount of time and space. When descriptive notes and a pelvic organ prolapse map are added, a more complete description of the prolapse can be created. By dividing the vagina through a coronal plane, tridimensional anatomy can be simplified to two dimensions. The extent of prolapse is recorded using a number (0 to 4)

at each six sites in the vagina. Two sites are located on the anterior, superior and posterior walls of the vagina, respectively. The six numbers are recorded as a measure of descent. For all sites except the perineum, the hymen is used as a fixed anatomic reference point. Zero indicates a normal anatomic position for a site, whereas 4 represents maximum prolapse. Between these extremes, the intervening numbers grade descent using a halfway system. The examination is performed with the patient straining so that maximum descent is attained. The perineum is graded using the familiar perineal laceration system used in obstetrics. The patient is asked to hold or strain to evaluate the amount of muscular and fascial support. Comments may include site of dominant prolapse, location of scars, palpable plications, and the type of efforts necessary to demonstrate maximum prolapse. Strength of the levator ani contraction may be recorded as 0 to 4.

Bump (1996) and colleagues presented a standard system of terminology (POP-Q) recently approved by the International Continence Society, the American Urogynecologic Society, and the Society of Gynecologic Surgeons for the description of female pelvic organ prolapse and pelvic floor dysfunction. An objective site–specific system for describing, quantifying, and staging pelvic support in women is included. It has been developed to enhance both clinical and academic communication regarding individual patients and populations of patients. Clinicians and researchers caring for women with pelvic organ prolapse and pelvic floor dysfunction are encouraged to learn and use the system.

V. Physical Examination of the Patient with POP

Physical examination is an integral part of the evaluation of the patient with POP. In the lithotomy position, the woman is asked to bear down (Valsalva) while the examiner evaluates the degree of prolapse visually, manually and with a speculum. In some women in whom prolapse is reported but not seen on examination, the examination can be repeated in the standing position. In some cases when prolapse is still apparent, the patient can return at a later time during the day for reevaluation. POP can also be evaluated with imaging studies. Fluoroscopic evaluation with proctography or defacography with barium enema has been utilized. Perineal ultrasound can also be utilized in the assessment of POP. MRI has also been utilized to evaluate POP and can further evaluate urethral abnormalities such as urethral diverticulitis.

It is important to assess the health of the vaginal epithelium in the post menopausal patient. In the setting of post menopausal urogenital atrophy with POP, consideration can be given to the use of transvaginal estrogen therapy. It is believed that topical estrogen may improve epithelial blood flow and promote vaginal healing after surgery. Karp (2012) randomized 45 women to estrogen ring versus placebo estrogen ring versus control group immediately after POP repair. At 12 weeks postoperatively, the estradiol ring group had a significantly improved maturation value and objective atrophy assessment compared with the placebo ring and control arms. In addition, granulation tissue was increased in the placebo ring arm. Finally, they noted subjective atrophy scores did not differ among the groups. They concluded that early administration of vaginal estrogen after vaginal surgery via an estradiol-releasing ring is feasible and

results in improved markers of tissue quality postoperatively compared to placebo estrogen ring and control group.

VI. Surgical Treatments for prolapse

Treatments for prolapse are multiple and can include plication based repairs (Kelly), anterior and posterior colporrhaphies, uterosacral spinous ligament fixations, sacrospinous ligament fixations, biological graft interposition, and mesh based interposition grafts (abdominal sacrocolpopexy and vaginal mesh based grafts).

1. Mesh vs. Biologic Repairs.

Culligan (2005) compared the objective anatomic outcomes after sacral colpopexy performed with cadaveric fascia lata and polypropylene mesh. They utilized POP-Q for evaluation. 100 patients were randomized to receive either fascia (n = 46) or mesh (n = 54). Of the 89 patients returning for 1-year follow-up, 91% (41/45) of the mesh group and 68% (30/44) of the fascia group were classified as objectively cured (P = .007). The authors noted significant differences between the mesh and fascia groups with respect to the 1-year postoperative comparisons of points Aa, C, and POP-Q stage. There were no differences between the 2 groups with respect to points TVL (total vaginal length), GH (genital hiatus), PB (perineal body), Ap or Bp (2 points along the posterior vaginal wall). They concluded that polypropylene mesh was superior to fascia lata in terms of POP-Q points, POP-Q stage, and objective anatomic failure rates.

Flynn (2005) evaluated 1-year outcomes of sacrocolpopexy with the use of allograft fascia lata. Patients underwent pre- and postoperative evaluation of prolapse

with the POP-Q. 24 patients were studied. No significant intraoperative or postoperative complications or graft erosions occurred. Prolapse of stage 2 or more in compartments Aa, Ba, Ap, Bp, and C was preoperatively 50%, 74%, 78%, 84%, and 68% and postoperatively 11%, 16%, 21%, 26%, and 5%, respectively. The authors concluded that allograft fascia lata may be a suitable alternative to permanent mesh for sacrocolpopexy, but agreed that longer-term outcomes and larger studies are needed.

Weber (2001) sought to compare outcomes after anterior colporrhaphy with the use of 3 different surgical techniques. They evaluated 114 women with anterior vaginal prolapse who were randomly assigned to undergo anterior repair by one of 3 techniques: standard, standard plus polyglactin 910 mesh, or ultralateral anterior colporrhaphy. Of 114 patients who were originallyenrolled, 109 patients underwent operation, and 83 patients (76%) returned for follow-up. Mean age (+/- SD) was 64.7 +/- 11.1 years. At entry, 7 patients (7%) had stage I anterior vaginal prolapse; 35 patients (37%) had stage II anterior vaginal prolapse; 51 patients (54%) had stage III anterior vaginal prolapse; and 2 patients (2%) had stage IV anterior vaginal prolapse. At a median length of follow-up of 23.3 months, 10 of 33 patients (30%) who were randomly assigned to the standard anterior colporrhaphy group experienced satisfactory or optimal anatomic results, compared with 11 of 26 patients (42%) with standard plus mesh and with 11 of 24 patients (46%) with ultralateral anterior colporrhaphy. The severity of symptoms that were related to prolapse improved markedly (preoperative score, 6.9 +/- 2.7; postoperative score, 1.1 +/- 0.8). Twenty-three of 24 patients (96%) no longer required manual pressure to void after operation. The authors concluded that all 3 techniques of anterior colporrhaphy provided similar anatomic cure rates and symptom resolution for

anterior vaginal prolapse repair. The addition of polyglactin 910 mesh did not improve the cure rate compared with standard anterior colporrhaphy.

Sand (2001) evaluated the efficacy of polyglactin 910 mesh in preventing recurrent cystoceles and rectoceles. 161 patients were evaluated. After 1 year, 30 (43%) of 70 subjects without mesh and 18 (25%) of 73 subjects with mesh had recurrent cystoceles beyond the mid-vaginal plane (P =.02). Eight women without mesh and 2 women with mesh had recurrent cystoceles to the hymenal ring (P =.04). No recurrent cystoceles beyond the hymenal ring occurred in either group. Multivariate logistic regression analysis showed concurrent slings to be associated with significantly fewer recurrent cystoceles (odds ratio, 0.32; P =.005), whereas the presence of mesh remained significantly predictive of fewer cystocele recurrences in this analysis. Thirteen recurrent rectoceles were noted 1 year postoperatively, with no differences between groups. The authors concluded that Polyglactin 910 mesh was found to be useful in the prevention of recurrent cystoceles.

2. Biologic repair with graft versus no graft in the anterior compartment.

Guerette (2009) and colleagues sought to compare outcomes of anterior colporrhaphy alone to that reinforced with bovine pericardium graft. 94 patients were enrolled. 72 (77%) were followed for 1 year and 59 (63%) were followed for 2 years. Postoperative complications were low in both groups (10 in bovine pericardium graft and 16 in anterior colporrhaphy alone). One year after surgery, successful anterior vaginal wall support was obtained in 85% of the bovine pericardium graft group and 78% of anterior colporrhaphy-alone group (P=.544). For the group with 2-year analyses, the

success rate was 76% for the bovine pericardium graft group and 63% for anterior colporrhaphy-alone group (P=.509). Postoperative Urogenital Distress Inventory-6 and POP-UISFQ-12 scores were uniformly improved over baseline in both groups. The authors concluded that the use of bovine pericardium graft for anterior vaginal prolapse does not have higher complication rates or healing difficulties. At 1- and 2-year follow-up, anterior colporrhaphy with bovine pericardium reinforcement did not show a statistically significant improvement over colporrhaphy alone.

Meschia (2007) evaluated the efficacy of the Pelvicol porcine collagen implant for preventing recurrent anterior vaginal wall POP. They studied 201 (98 implant group; 103 no implant group) women with stage II or greater anterior vaginal wall prolapse (point Ba -1 or greater) according to the POP-Q. The patients were randomly assigned to undergo anterior vaginal repair or the same procedure with Pelvicol implant reinforcement. At 1-year follow up visit, most women were satisfied with the postoperative condition with a significant decrease in the visual analog scale score in each group ($p < 0.001$). Anatomical anterior recurrence (point Ba greater than -1) was observed in 7 women (7%) in the implant group and in 20 (19%) in the other groups (OR 3.13, 95% CI 1.26-7.78, $p = 0.019$). Additionally, there were 11 women (3 and 8, respectively, or 5%) with posterior recurrence and 6 (3 per group or 3%) with unsatisfactory results at the upper vaginal segment. One patient who received a porcine implant had vaginal extrusion of the graft 1 month after surgery. The authors concluded that the Pelvicol implant can be easily and readily used to augment and reinforce anterior colporrhaphy. The reported prolapse recurrence rate was considerably lower in the implant group compared with outcomes in patients treated with simple anterior repair.

Groutz (2001) reported their results in which cadaveric fascia lata is used for cystocele repair. They studied 21 consecutive women (mean age 67 +/- 10 years) with severe cystocele were prospectively enrolled. Solvent-dehydrated, Tutoplast-processed, cadaveric fascia lata was used for cystocele repair. Of the 21 patients, 19 underwent concomitant PVS, 3 concomitant vaginal hysterectomy, and 8 posterior colporrhaphy in addition to their cystocele repair. The mean follow-up was 20 +/- 6 months (range 12 to 30). No postoperative complications related to the material or technique occurred. None of the patients developed a recurrent cystocele. None of the patients developed postoperative de novo urge incontinence or dyspareunia. The authors concluded that the use of solvent-dehydrated cadaveric fascia lata for cystocele repair, as well as PVS, is associated with encouraging short and medium-term results. They suggested that long-term follow-up is needed to evaluate whether these results are durable.

3. Biologic repair with graft versus no graft in the posterior compartment.

Paraiso (2006) evaluated the outcomes of 3 different rectocele repair techniques. They studied 106 women with stage II or greater posterior vaginal wall prolapse were randomly assigned to either posterior colporrhaphy (n = 37), site-specific rectocele repair (n = 37), or site-specific rectocele repair augmented with a porcine small intestinal submucosa graft (n = 32). Of 106 subjects who enrolled, 105 underwent surgery and of those, 98 subjects returned (93%) with a mean follow-up of 17 +/- 7 months. After 1 year, those subjects who received graft augmentation had a significantly greater anatomic failure rate (12/26; 46%) than those who received site-specific repair alone (6/27; 22%) or posterior colporraphy (4/28; 14%), P = .02. There was a significant improvement in

prolapse and colorectal scales and overall summary scores of the Pelvic Floor Distress Inventory short form 20 (PFDI-20), the Pelvic Floor Impact Questionnaire short form 7 (PFIQ-7) after surgery in all groups ($P < .001$ for each) with no differences between groups. The proportion of subjects with functional failures was 15% overall, and not significantly different between groups. There was no significant change in the rate of dyspareunia 1 year after surgery and there were no differences between groups. Overall sexual function as measured by the PISQ-12 improved significantly in all groups postoperatively ($P < . 001$), with no differences between groups. The authors concluded that posterior colporraphy and site-specific rectocele repair result in similar anatomic and functional outcomes. The addition of a porcine-derived graft does not improve anatomic outcomes.

4. Abdominal Sacrocolpopexy with mesh

Nygaard (2004) conducted a literature search on MEDLINE using Ovid and PubMed, from January,1966 to January, 2004, using search terms "sacropexy," "sacrocolpopexy," "sacral colpopexy," "colpopexy," "sacropexy," "colposacropexy," "abdominal sacrocolpopexy" "pelvic organ prolapse and surgery," and "vaginal vault prolapse or surgery" and included articles with English-language abstracts. They determined that the success rate, when defined as lack of apical prolapse postoperatively, ranged from 78-100% and when defined as no postoperative prolapse, from 58-100%. The median reoperation rates for POP and for SUI in the studies that reported these outcomes were 4.4% (range 0-18.2%) and 4.9% (range 1.2% to 30.9%), respectively. The overall rate of mesh erosion was 3.4% (70 of 2,178). They noted that some reports found

more mesh erosions when concomitant total hysterectomy was done, whereas other reports did not. They found no data to either support or refute the contentions that concomitant culdoplasty or paravaginal repair decreased the risk of failure. They recommended burying the graft under the peritoneum to attempt to decrease the risk of bowel obstruction; despite this, the median rate of SBO requiring surgery was 1.1% (range 0.6% to 8.6%). They concluded that sacrocolpopexy is a reliable procedure that effectively and consistently resolves vaginal vault prolapse. They stressed that patients should be counseled about the low, but present risk, of reoperation for prolapse, stress incontinence, and complications.

Nygaard (2013) described anatomic and symptomatic outcomes up to 7 years after ASC, and to determine whether these are affected by concomitant anti-incontinence surgery (Burch urethropexy) in the extended CARE study. The authors noted that by year 7, the estimated probabilities of treatment failure (POP, SUI, UI) from parametric survival modeling for the urethropexy group and the no urethropexy group, respectively, were 0.27 and 0.22 for anatomic POP (treatment difference of 0.050; 95% CI, -0.161 to 0.271), 0.29 and 0.24 for symptomatic POP (treatment difference of 0.049; 95% CI, -0.060 to 0.162), 0.48 and 0.34 for composite POP (treatment difference of 0.134; 95% CI, -0.096 to 0.322), 0.62 and 0.77 for SUI (treatment difference of -0.153; 95% CI, -0.268 to 0.030), and 0.75 and 0.81 for overall UI (treatment difference of -0.064; 95% CI, -0.161 to 0.032). Mesh erosion probability at 7 years (estimated by the Kaplan-Meier method) was 10.5% (95% CI, 6.8% to 16.1%). The authors concluded that during 7 years of follow-up, ASC failure rates increased in both groups. Urethropexy prevented SUI longer than no urethropexy performed. Finally, they noted that ASC effectiveness should

be balanced with long-term risks of mesh or suture erosion.

Brubaker (2007) reported the anatomic and functional outcomes 2 years after sacrocolpopexy in stress-continent women with or without prophylactic Burch colposuspension. Their analysis is based on 302 of 322 randomized participants. Most were Caucasian (94%), with a mean age of 62+/-10 years (mean+/-standard deviation). Two years after surgery, 32.0% and 45.2% of women in the Burch and control groups, respectively, met the stress incontinence endpoint (presence of symptoms or positive cough stress test or interval treatment for stress incontinence, P=.026). The apex was well supported (point C within 2 cm of total vaginal length) in 95% of women, and this was not affected by concomitant Burch (P=.18). There was a trend toward fewer urgency symptoms in the Burch group (32.0% versus 44.5% no Burch, P=.085). Twenty participants experienced mesh or suture erosions. They concluded that the early advantage of prophylactic Burch colposuspension for SUI that was seen at 3 months remains at 2 years. Apical anatomic success rates were high and not affected by concomitant Burch.

VII. Role for Mesh in Pelvic Organ Prolapse Repairs

Synthetic mesh was initially used in the surgical repair of abdominal wall hernias because of their ability to bolster tissue support in cases where native tissue is somewhat weaker. However, known unique risks to mesh involve erosion and rejection. For approximately 30 years, synthetic mesh has also been used in gynecologic surgery. Iglesia (1997) evaluated the use of mesh in surgical procedures from 1960 to 1965. They concluded that long-term success of ASC using mesh ranges from 68% to 100%. Mesh-

related complications rates included a 9% erosion rate. These mesh erosions are not unique to pelvic floor surgery. Bauer (1999) reported their experience with PTFE to repair abdominal wall defects with 12-year follow up. 98 patients were studied with half undergoing repeat surgery for hernia repair. Their results indicate that prosthetic patches of PTFE are safe and effective when used in the repair of large abdominal wall defects that cannot be closed primarily. Their operative complications were within acceptable limits, as was the re-herniation rate. With regard to mesh erosions of permanent mesh, several factors are thought to be implicated including: poor healing environment influenced by nutritional status and blood flow, infections, foreign body reactions, and mesh characteristics such as rigidity, mesh density, and mesh porosity.

The Gynemesh PS mesh used in Prolift is an excellent synthetic mesh to be used in pelvic floor surgery. First, it is dynamic and has just the right amount of rigidity and flexibility. This allows it to mold well into the vaginal wall. It is able to conform to the tissues of the vaginal wall without placing too much tension in the area and also allow the surrounding tissues to function normally. The mesh is light weight and allows for good structural integrity to support native tissue. Gynemesh PS has the necessary tensile strength to provide the pelvic floor support and significantly reduce the risk of prolapse recurrence, especially in the anterior compartment. A chart from the Gynemesh PS White Paper describes the following mesh characteristics:

TABLE 1:
Mesh Characteristics

Characteristic	GYNEMESH PS	PROLENE Mesh	MERSILENE Mesh
Thickness (in)	0.016	0.019	0.010
Unit Weight (mg/cm^2)	4.36	7.60	4.22
Porosity (% of total area)	65.6	53.1	62.7
Burst Strength (psi)	115.82	234.33	82.92
Flexibility (mg/cm)	176.71	623.53	17.41
Tear Strength (lb)			
W (knitting machine axis)	4.41	7.32	1.23
C (across machine axis)	2.56	9.03	1.27
Suture Pull-Out (lb)			
W (knitting machine axis)	5.96	11.22	2.27
C (across machine axis)	6.55	13.88	2.06
Tensile Strength (lb)			
W (knitting machine axis)	21.67	50.48	26.37
C (across machine axis)	21.78	42.32	13.39

As evidenced by various curricula from professional societies, residents, fellows, and pelvic floor surgeons are expected to be familiar with graft/mesh properties, complications associated with graft repairs and how to manage complications from graft repairs, and be able to discuss the alternatives, risks, benefits, complications, success rates, and levels of evidence for mesh and non-mesh based repairs. (FPMRS Study Materials; ABOG and ABU Guide to Learning in FPMRS; ACGME Program Requirements for Graduate FPMRS; AUA National Medical Student Curriculum; AUGS Resident Learning Objectives; and IUGA Guidelines for Training in FPMRS).

Gynemesh PS is made from the same Prolene material used in the Prolene sutures, Prolene mesh, and Prolene TVT products, but it uses a 3.5 mil Prolene fiber, which has a slightly smaller fiber diameter than the TVT which uses a 6 mil Prolene fiber. Gynemesh PS is considered a macroporous, monofilament, polypropylene, Amid Type 1 mesh. The pore size of Gynemesh PS is commonly cited as being 2.4mm (or 2,400 microns), which

is considered large pore, and is significantly larger than the 75 microns necessary to allow for the in-growth of blood vessels and interaction with other tissues. Microscopically, there will be ingrowth of blood vessels, fibroblast proliferation and collagen fiber integration into the mesh structure. These promote integration of the mesh into the normal vaginal wall as well as promote healing. Further, through this healing and tissue integration process, inflammation may be halted and infection inhibited. This leads to increased mobility of the repaired tissue. Gynemesh PS is a large pore, monofilament mesh. This is in contrast to multifilament meshes, which have small pore size and thus allow bacteria to enter the mesh structure and actually prevent a neutrophilic cellular response. This latter process can cause infections around the mesh. There are no reliable clinical studies that have confirmed plaintiffs' experts' theory that Gynemesh PS mesh undergoes pore collapse in vivo.

Maher (2016) sought to evaluate transvaginal mesh grafts versus native tissue repair for vaginal prolapse in a level 1 Cochrane Review. They sought to study this question because POP affects nearly 50% of women who have had children. They evaluated 37 randomized controlled trials comprised of 4,023 women comparing transvaginal grafts versus traditional native tissue repair for repairing vaginal prolapse through the time period to July 2015. The authors noted low to moderate quality evidence suggesting that there are advantages to using transvaginal permanent mesh compared to native tissue repair. Some of the advantages included: lower rates of awareness of prolapse, need for reoperation for prolapse, and recurrent prolapse on physical examination. The authors noted that if 19% of women are aware of prolapse after native tissue repair, 10-15% will be aware of prolapse after permanent mesh repair.

They further noted that if the rate of recurrent prolapse on examination after a native tissue repair is 38%, the risk would be 11-20% after a repair with transvaginal permanent mesh.

Maher (2016) did indicate that there are also problems associated with permanent transvaginal mesh. If the reoperation rate for prolapse, urinary incontinence, or mesh exposure after native tissue repair is assumed to be 5%, the risk would be 7-18% after permanent mesh repair. They noted that 8% of women in the mesh group required repeat surgery for mesh exposure. Maher (2016) also found that absorbable mesh may reduce the risk of recurrent prolapse on examination compared to native tissue repair, but there is insufficient evidence on absorbable mesh for us to draw any conclusions for other outcomes. The authors noted there is no difference between biological grafts and native tissue repair on rates of awareness of prolapse or reoperation for prolapse. Maher (2016) indicated that while permanent mesh has some advantages over native tissue, there are also disadvantages in its routine use. They suggested that many transvaginal permanent meshes were withdrawn from use in 2011, and the newer, lightweight transvaginal permanent meshes still available have not been evaluated within a randomized study.

Maher (2013) performed a systematic review of post operative sexual function after POP repair. Fifty-six randomized controlled trials were identified evaluating 5954 women. For upper vaginal prolapse (uterine or vault) ASC was associated with a lower rate of recurrent vault prolapse on examination and painful intercourse than with vaginal sacrospinous colpopexy. These benefits must be balanced against a longer operating time, longer time to return to activities of daily living and increased cost of the abdominal approach. In single studies the ASC had a higher success rate on examination and lower

reoperation rate than high vaginal uterosacral suspension and transvaginal polypropylene mesh.

The Schimpf (2016) Systematic Review from the Society of Gynecologic Surgeons Systematic Review Group concluded that the use of synthetic mesh augmentation of anterior wall POP repair improves anatomic outcomes and bulge symptoms compared with native tissue repair. In addition, there was improvement in other subjective outcomes, including urinary incontinence or dyspareunia in both groups without preference for one over the other. The SGS Review noted that the use of a biologic graft or synthetic absorbable mesh use did not provide an advantage in any compartment. With respect to mesh erosions/exposures, mesh erosion rates ranged from 1.4-19%, with most of these treated in the office, at the anterior vaginal wall, but 3-36% when mesh was placed in multiple compartments. Further, operative mesh revision rates ranged from 3-8%. The authors concluded that there is high-quality evidence that the use of synthetic nonabsorbable mesh improves anatomic outcomes compared with native tissue anterior colporrhaphy. Data from meta-analyses confirm that mesh repairs alsoprovided superior relief of subjective bulge symptoms. Finally, Schimpf concluded that there is also high-quality evidence to suggest no difference for subjective outcomes including quality of life and urinary and sexual function.

Mesh-based repair prolapse studies and results

Altman (2011) performed a multicenter, parallel-group, randomized, controlled trial, comparing the use of a trocar-guided, transvaginal polypropylene-mesh repair kit with traditional colporrhaphy in women with prolapse of the anterior vaginal wall

(cystocele). The primary outcome was a composite of the objective anatomical designation of stage 0 (no prolapse) or 1 (position of the anterior vaginal wall more than 1 cm above the hymen), according to the POP-Q system, and the subjective absence of symptoms of vaginal bulging 12 months after the surgery. Of 389 women who were randomly assigned to a study treatment, 200 underwent prolapse repair with the transvaginal mesh kit and 189 underwent traditional colporrhaphy. At 1 year, the primary outcome was significantly more common in the women treated with transvaginal mesh repair (60.8%) than in those who underwent colporrhaphy (34.5%). The procedure took longer to perform and the rates of intraoperative hemorrhage were higher in the mesh-repair group than in the colporrhaphy group ($P<0.001$ for both comparisons). Rates of bladder perforation were 3.5% in the mesh-repair group and 0.5% in the colporrhaphy group ($P=0.07$), and the respective rates of new stress urinary incontinence after surgery were 12.3% and 6.3% ($P=0.05$). In addition, surgical reintervention to correct mesh exposure during follow-up occurred in 3.2% of 186 patients in the mesh-repair group. The authors concluded that mesh based repairs for POP were efficacious with acceptable complications not unexpected for that procedure.

Gagnon (2010) reported their 21-month follow up using Prolift for POP repair. 56 patients were evaluated. Their mean age was 68 years with a BMI of 27 and parity average of 3. Previous POP repair had been performed in 17 patients (30%) and a hysterectomy in 43 (77%). With a median follow-up of 21 months, the authors noted the cure rate for POP was 91% (48/53) and the reoperation rate was 8% (4/53). Their perioperative complications included 1 rectal laceration and 1 case of prolonged bleeding. Their short-term postoperative complications included 10 episodes of transient urinary

retention that required immediate tape release in 4 patients. Their long-term complications included 5 POP recurrences. They concluded that the Prolift system appears to be a relatively safe and effective alternative to conventional surgeries for the treatment of recurrent or high-grade multiple compartment POP.

Hwang (2011) reported their medium- to long-term outcome of transvaginal pelvic reconstructive surgery using the Prolift system for POP. 65 patients were followed for 1 to 3 years postoperatively. Assessment included pre- and postoperative POP-Q stage, UDI-6 and IIQ-7 scores. The overall anatomic success rate was 97% after a median of 24.5 months and 94% for the 34 women followed for more than 2 years. POP-Q stage, UDI-6, and IIQ-7 scores all improved significantly after surgery. The authors reported the following complications: one bladder perforation (1.5%) and one bowel perforation (1.5%), prolonged catheterization in four patients (6%), and mesh erosion in one (2%). Eight received a blood transfusion (12%). The authors concluded that Prolift surgery for POP yielded a good anatomical outcome and satisfactory symptom improvement that appeared to be durable after 2 years.

Nair (2011) reported anatomic outcomes at 2 years in patients who underwent transvaginal mesh repair using Prolift for POP. Their prospective study of 60 women had a mean age of 57.5 years and median follow up of 29 months. They noted significant improvements in POP-Q measurements of point C/D and the leading edge of the prolapse/most dependent part of the vagina ($p<0.001$). Their overall anatomic success rate was 85%. Mesh exposure was noted in 15% of patients and recurrent prolapse in 10%. They concluded that the procedure offered good anatomical success rate over the medium term (29 months). The authors emphasized the need for long-term follow-up in

these patients to check for mesh erosion. This complication was already well known to physicians with data published on this over 10 years prior to this paper.

Gutman (2013) presented their 3-year outcomes of a double-blind, multicenter, randomized trial comparing vaginal prolapse repair with and without mesh. They randomized patients to traditional vaginal prolapse surgery without mesh and vaginal colpopexy repair with mesh. They evaluated anatomic, symptomatic, and combined cure rates for those with at least 3-year validated quality-of-life questionnaires and 2- or 3-year postoperative blinded POP-Q examination. 65 women were enrolled (33 mesh, 32 no mesh) before the study was prematurely halted as a result of a 15.6% mesh exposure rate. At 3 years, 51 of 65 (78%) had quality-of-life questionnaires (25 mesh, 26 no mesh) and 41 (63%) had examinations. Three participants died, three required reoperation for recurrent prolapse (all in mesh group), and eight were lost to follow- up. No differences were observed between groups at 3 years for prolapse stage or individual prolapse points. Stage improved for each group (90% and 86%) from baseline to 3 years (P<.01). Symptomatic improvement was observed with no differences in scores between groups. Cure rates did not differ between groups using a variety of definitions, and anatomic cure was lowest for the anterior compartment. The authors concluded that there was no difference in 3-year cure rates when comparing patients undergoing traditional vaginal prolapse surgery without mesh with those under- going vaginal colpopexy repair with mesh.

Benbouzid (2012) reported their 4.5 year experience with the Prolift system. This is a retrospective study of patients who underwent POP repair by two experienced surgeons. 75 patients were evaluated with a mean follow up of 53.7 ± 8.8 months (range

36-72 months). Patients were treated with two-arm Prolift posterior, four-arm Prolift anterior and six-arm Prolift total in three (4%), 51 (69%) and 21 (27%) cases, respectively. At last follow up, 64 (85%) patients were cured, with no POP recurrence. Mesh exposure occurred in four (5%) patients. The Pelvic Floor Distress Inventory-20 symptom score was low at last follow up (median 8, range 3-18), in accordance with objective cure data. They concluded that the Prolift repair provided long term prolapse reduction with an acceptable side effect profile.

Kozal (2014) reported their 7-year follow up data using Prolift for POP repair. They retrospectively analyzed a cohort of 112 consecutive patients who underwent the Prolift procedure since 2006. The median follow-up was 49.5 months (range: 16-85). Total mesh was used in 32 patients (29%), an isolated anterior mesh in 57 patients (51%) and an isolated posterior mesh in 23 patients (21%). Concomitant surgical procedures were performed for 44 patients (39%). Overall, 72% (18/25) of the complications were managed medically. They reported a failure rate of 8% (n = 9) occurring after a median follow-up of 9.5 months (range: 1-45). Among the 64 patients who had preoperative sexual activity (57%), de novo dyspareunia occurred in 9 patients (16%). The authors concluded that despite its market withdrawal, the Prolift system was associated with good midterm anatomic outcomes and few severe complications.

Nussler (2015) sought to compare the results of primary anterior vaginal wall prolapse repair, using standard anterior colporrhaphy or non-absorbable mesh in a routine health care setting. 6,247 women had an anterior colporrhaphy, and in 356 a non-absorbable mesh was used. The 1-year cure rate for the mesh group was superior to that of the colporrhaphy group with an odds ratio (OR) of 1.53 (CI 1.1-2.13. Patient

satisfaction, OR = 2.45 (CI 1.58-3.80), and patient improvement, OR 2.99 (CI 1.62-5.54), was also higher in the mesh group. However, patient-reported complications, OR = 1.51 (CI 1.15-1.98), and the incidence of persisting loin pain, OR = 3.58 (CI 2.32-5.52), were also higher in the mesh group as were surgeon-reported complications, OR = 2.27 (CI 1.77-2.91), bladder injuries, OR = 6.71 (CI 3.14-14.33), and re-operations within 12 months, OR = 6.87 (CI 3.68-12.80). The authors concluded that mesh reinforcement, in primary anterior vaginal wall prolapse patients, enhanced the likelihood of anatomical success at 1 year after surgery. However, mesh implant was associated with a significantly higher incidence of bladder injury, and reoperations. Both patient- and surgeon-reported complications noted more patient-reported pain and a longer hospital stay.

Meyer (2016) and colleagues reported their long-term objective and subjective outcome of Prolift between 2006 and 2008 with a minimum 5 year follow up. The authors noted improvement in POP-measurements post-operatively. PISQ scores were similarly improved. 85% of patients were somewhat to completely satisfied. 3 patients (6%) experienced mesh exposure and 25 (36%) experienced dyspareunia. The authors concluded that POP repair using synthetic mesh resulted in positive objective and subjective outcomes with significantly improved QOL at a minimum 5 year follow up interval.

Heinonen (2016) reported their long-term subjective and objective outcomes after the transvaginal mesh using the Prolift system with 7 year follow up. Objective outcome was assessed using the POP-Q system using two definitions: POP-Q stage ≤ 1, and vaginal wall prolapse at or above the hymen or vaginal apex not descending below the

upper third of the vagina. Of 195 patients, 161 (82%) participated this study after a median of 7 years. The scores in questionnaires evaluating UI or FI and constipation or pelvic floor symptoms indicated favorable surgical outcomes. 80% of patients were satisfied with the procedure. Anatomical cure was 56-69% depending on the definition used. Reoperation due to POP in any compartment was performed in 16% of patients. Mesh exposure rate was 23%, most of these being asymptomatic and of late onset. The authors concluded that the outcome of the Prolift procedure was satisfactory. Subjective cure was superior to anatomical cure. Most mesh exposures observed were in the long-term and were asymptomatic.

Prolift and Sexual Health; Prolift+M; Prolift Complications

Withagen (2009) completed a prospective chart study with 2 centers to evaluate patients undergoing the Prolift procedure for POP. They utilized the Urogenital Distress Inventory and the Incontinence Impact Questionnaire with some additional questions regarding sexual function. 118 patients were studied. They found a significant improvement in patient's ability to have sexual intercourse postoperatively. There were no significant differences in dyspareunia during intercourse and no differences when the pre and postoperative diameter of the vagina was evaluated. Thus, there was no vaginal narrowing that caused any significant difficulties with intercourse. There was no increase in dyspareunia.

Bhatia (2012) evaluated patients undergoing POP repair using Prolift+M versus age-matched, sexually active controls that underwent the standard Prolift procedure. 71 patients (n=39 standard mesh, n=32 +M mesh) at 4 months and 40

patients (n=20 standard mesh, n=20 +M mesh) at 1 year had completed both preoperative and postoperative PISQ forms. In comparing both groups, there is a significant improvement in postoperative sexual desire (PISQ #1), comfort with intercourse (PISQ #5), and overall sexual function (Total PISQ Score) with the hybrid mesh compared to the standard mesh at 4 months but this significance was not found at 1 year postoperatively. Total PISQ scores also increased significantly in both groups between 4 months and 1 year post-operatively. This improvement was greater in the standard mesh group but was not significant. The authors concluded that when a hybrid mesh composed of permanent and absorbable fibers is used, compared to the traditional all-polypropylene mesh, the improvement in sexual health appears to be greater in the short-term, however, there is no significant difference at 1 year.

Milani (2012) and colleagues reported on 128 subjects with POP who underwent the Prolift+M system, and they found excellent anatomical success. The QOL measures including pelvic symptoms and sexual function improved significantly from baseline ($p<0.001$). 96.9 % subjects responded much better or a little better in the PGI-C. Mesh exposure was observed in 19 subjects over 3 years (14%); 14 (10%) occurred within the first 12 months post surgery. 10 of 19 exposures were at the apex, the majority following a total repair; 15 resolved on partial mesh excision (10 in-office and 5 excised in the operating room) while 4 subjects had ongoing mesh exposure at 3 years (≤1 cm in size), being treated conservatively. The incidence of mesh exposure varied between sites (0–20%). At 3 years, no subjects had de novo pelvic pain; 3 (3%) had pain only on mesh palpation during pelvic examination. Resolution of pre-existing pelvic pain occurred in 7 (6%) subjects. De novo dyspareunia was observed in 3/33 subjects (9%); the causes were

vaginal atrophy; uterine prolapse and 1 unknown. None of these subjects had mesh exposures. Pre-existing dyspareunia resolved in 6/18 (33%) subjects. The authors concluded that transvaginal mesh repair with a partially absorbable mesh yields sustained anatomic and functional results. No major safety concerns were identified, and there was a low incidence of pain and dyspareunia.

Quemener (2014) reported their experience with Prolift+M partially absorbable mesh to evaluate reoperation after transvaginal POP repair. 250 patients were studied with median follow up of 20 months. The global reoperation rate was 8%. The authors compared this data with their previously reported data for nonabsorbable mesh. When comparing the rates of reintervention at 12 and 18 months, there was no difference between the groups (Prolift+M versus Prolift) for mesh related complications including mesh exposure. Further, there was no difference in terms of prolapse recurrence and urinary complications. The authors concluded that their study did not show that partially absorbable Prolift+M mesh significantly changed any of the abovementioned parameters. Finally, rates of reintervention for recurrence were comparable with those reported after nonabsorbable mesh.

Plaintiffs' experts' opinions associating an inflammatory response with chronic pelvic pain are not reliable, especially their reliance on animal studies when much higher level clinical evidence is available. They also neglect to account for the conclusions of several studies which have demonstrated that pain is not directly correlated to an inflammatory response. (Klein-Patel 2011; Hill 2015; Klosterhalfen 2002).

de Landsheere and Cosson (2012) performed a retrospective study of Prolift mesh evaluating the global reoperation rates and complications. 600 patients were

identified and followed for a period of 15 to 63 months. The global reoperation rate was 11.6%. Indications were incontinence surgery in 6.9%, mesh related complications in 3.6% or prolapse recurrence in 3%. The details of their postoperative reoperation indications, rates, presentation time and management were studied in detail. With a mean presentation time of 15 months and a range of 0.5 to 49 months, mesh exposure occurred in 13/524 (2.5%) of patients. These were easily managed with partial mesh excision. Mesh exposures in the anterior compartment occurred in 5/421 (1.2%) and 8/476 (1.7%) and all were easily treated with partial mesh excision. Mesh infection occurred in only 1/524 (0.2%) of patients and occurred at a mean of 14 days post operatively. This was treated with total mesh excision. Mesh retraction with severe symptoms was similarly rare occurring in 2/524 (0.4%) of patients at a median of 14 months post operatively. Finally, rectal compression was similarly rare occurring in 2/476 (0.4%) of patients at a median of 18 months postoperatively. The authors concluded that the rates of mesh related complications and prolapse recurrence are relatively low with an experienced surgical team. The mesh exposure rate is low when compared to other studies where the rates were as high as 17%. The mesh exposure rate from Prolift mesh was comparable to that seen with sacrocolpopexy at 3.4%. Finally, the authors believe that mesh pain may not actually be due to the mesh but to a functional digestive disorder.

Gynemesh PS/Prolift Randomized Controlled Trials

Carey (2009) evaluated 139 women with stage 2 prolapse according to the POP-Q system requiring both anterior and posterior compartment repair. Subjects were

randomized to anterior and posterior vaginal repair with mesh augmentation (mesh group, n = 69) or traditional anterior and posterior colporrhaphy (no mesh group, n = 70). They found that at 12 month follow up, success in the mesh group was 81.0% (51 of 63 subjects) compared with 65.6% (40/61) in the no mesh group and was not significantly different (P-value = 0.07). A high level of satisfaction with surgery and improvements in symptoms and QOL data were observed at 12 months compared to baseline in both groups, but there was no significant difference in these outcomes between the two groups. Vaginal mesh exposure occurred in four women in the mesh group (5.6%). De novo dyspareunia was reported by five of 30 (16.7%) sexually active women in the mesh group and five of 33 (15.2%) in the no mesh group at 12 months. The authors concluded that vaginal surgery augmented by mesh did not result in significantly less recurrent prolapse than traditional colporrhaphy 12 months following surgery although there was a 15% improvement in success rate at 1 year with the mesh group.

Withagen (2011) sought to compare efficacy and safety of trocar-guided tension-free vaginal mesh insertion with conventional vaginal prolapse repair in patients with recurrent pelvic organ prolapse. 97 women underwent conventional repair and 93 mesh repair. The follow-up rate after 12 months was 186 of 190 patients (98%). Twelve months post surgery, anatomic failure in the treated compartment was observed in 38 of 84 patients (45.2%) in the conventional group and in eight of 83 patients (9.6%) in the mesh group (P<.001). Patients in either group reported less bulge and overactive bladder symptoms. Subjective improvement was reported by 64 of 80 patients (80%) in the conventional group compared with 63 of 78 patients (81%) in the mesh group. Mesh

exposure was detected in 14 of 83 patients (16.9%). The authors concluded that at 12 months, the number of anatomic failures observed after tension-free vaginal mesh insertion was less than after conventional vaginal prolapse repair. Symptom decrease and improvement of quality of life were equal in both groups.

El-Nazer (2012) sought to compare the clinical effectiveness of anterior colporrhaphy versus mesh repair as surgical management of anterior vaginal prolapse. 44 patients were evaluated and randomly recruited into two groups. Group I (23 patients) received anterior colporrhaphy, while group II (21 patients) received soft polypropylene mesh (GYNEMESH). Patients were followed for 2 years. They found that both groups showed clinical improvement in their symptoms and POP-Q staging at the end of the post-operative follow-up period. Improvement, however, was more significant in the repair with mesh group, as patients in this group reported better improvement of their prolapse symptoms, mainly vaginal bulge/pressure sensation ($P<0.05$), and showed better improvement in the anatomical staging, individual POP-Q points Aa and Ba (P\0.01), than the anterior colporrhaphy group. Group II also showed more satisfactory outcome with the general POP-Q staging ($P<0.05$) than group I, reflecting a better QOL of the patients in the repair with mesh group. They concluded that repair with mesh is superior to anterior colporrhaphy with more satisfactory outcome to the patients with short term follow up.

Halaska (2012) compared the recurrence and complication rates for sacrospinous fixation (SSLF) and prolene mesh techniques for the primary treatment of post hysterectomy vaginal vault prolapse. This was a multicenter, randomized, controlled study comparing SSLF or total mesh (Prolift). The examination included POP-Q,

urodynamics, ultrasound, and QOL questionnaires before and 3 and 12 months after surgery. 83 underwent SSLF and 85 mesh repair. Prolapse recurrence after 12 months occurred in 39.4% of the SSLF group and in 16.9% of the mesh group (PM< .003). The mesh exposure rate was 20.8%. No difference in QOL improvement as well as of denovo SUI and OAB onset was found. The authors concluded that mesh exposure occurrence was balanced against a lower POP recurrence rate in the patients undergoing mesh surgery compared with those undergoing SSLF.

Qatawneh (2013) evaluated the anatomical outcomes of a prospective randomized trial comparing tension-free polypropylene mesh-reinforced anterior vaginal prolapse with anterior colporrhaphy at the time sacrospinouscolpopexy and posterior fascial plication for the management of massive uterovaginal prolapse. A total of 116 patients with a stage III or IV (POP-Q/ICS) uterovaginal prolapse were randomized into two groups. The overall objective success rates (in all compartments) were 79% (42/53) in the mesh group and 62% (39/63) in the non-mesh group (p<0.043). The objective success rates in the anterior compartment was 85% (45/53) in the mesh group and 62% (39/63) in the non-mesh group (p<0.006). Three (6%) patients in the mesh group and 12 (19%) in the non-mesh group underwent repeat surgery for recurrent POP (p=0.03). The subjective success rates were 89% (47/53) in the mesh group and 76% (48/63) in the non-mesh group (p<0.08). The mean patient satisfaction rates with the surgery were 84% in the mesh group and 76% in the non-mesh group (p<0.08). The development of a UTI, right-sided buttock pain (temporary sciatic neuralgia) and new-onset SUI were not significantly different between the two groups. The mesh exposure rate was 8%. The authors concluded that transvaginal cystocele repair using tension-free polypropylene

mesh at the time of sacrospinous colpopexy and posterior fascial plication offers lower anatomic recurrence and less need for further prolapse surgery to correct recurrent pelvic floor defects than anterior colporrhaphy, sacrospinous colpopexy and posterior fascial plication.

da Silveira (2014) compared the outcomes of native vaginal tissue repair versus polypropylene mesh repair for the treatment of severe genital prolapse. Both groups were homogeneous preoperatively. There were no differences between the groups in operative time, complications or pain. At 1-year follow-up, anatomical cure rates were better in the mesh group in the anterior compartment (p=0.019). Significant improvement in QOL scores at 1-year follow up were observed in each group; between-group comparisons of changes in QOL scores revealed greater improvement in the mesh group. The authors concluded that both techniques were effective. However, anatomical efficacy was superior in the mesh group regarding the anterior compartment; QOL changes were also greater in the mesh group. However, complications were significantly higher in the mesh group.

Svabik (2014) compared Prolift Total vs unilateral vaginal sacrospinous colpopexy with native tissue vaginal repair (sacrospinous fixation, SSF). The primary outcome was anatomical failure based on clinical and ultrasound assessment. Seventy patients were randomized into two groups: 36 in the Prolift group and 34 in the SSF group. On clinical examination at 1-year follow-up, they observed one (3%) case of anatomical failure in the Prolift group and 22 (65%) in the SSF group (P<0.001). Using ultrasound criteria, there was one (2.8%) failure in the Prolift group compared with 21 (61.8%) in the SSF group (P<0.001). The postoperative POP score for subjective

outcome was 15.3 in the Prolift group vs 21.7 in the SSF group (P=0.16). The authors concluded that in patients with prolapse after hysterectomy and levator ani avulsion injury, SSF has a higher anatomical failure rate than does the Prolift Total procedure at 1-year follow-up.

As demonstrated in the level 1 RCTs comparing Prolift to traditional prolapse repairs, there was no statistically significant difference in vaginal length, de novo dyspareunia, sexual function, pelvic pain or quality of life. (Withagen 2011; Altman 2011; Sokol 2012/Gutman 2013; Halaska 2012; Svabik 2014; da Silviera 2014).

Dyspareunia and Pelvic Organ Prolapse Surgery

The relationship between pelvic floor surgery – with or without mesh - for prolapse and postoperative dyspareunia has been well-known to pelvic floor surgeons and described in the medical literature for decades. Francis (1961) noted that painful sexual intercourse is commonly found after operations for prolapse. The author felt that approximately 50 per cent of women do not have intercourse at all or do so infrequently and with discomfort following operations of this type. The author believes that 50% of these cases are due to loss of libido on the part of either sexual partner with some cases due to male impotence. Further, 25% of married women who had POP repair or operations such as vaginal hysterectomy have, for various reasons, stopped having intercourse before their procedure. In addition, a certain number of patients avoid coitus following these operations because they are afraid that harm will result.

Khan (1997) noted that long term sexual dysfunction after posterior colporrhaphy has many causes: increasing age and postmenopausal atrophy together with vaginal

surgery may cause sexual dysfunction. In their study of 231 patients, they noted that postoperatively, prolapse symptoms due to rectocele decreased (64% vs 31 %). Constipation (22% vs 33%), incomplete bowel emptying (27% vs 38%), incontinence of feces (4% vs 11%) and sexual dysfunction (18% vs 27%) increased. In addition, those with incontinence of stool were more likely to have had two or more posterior colporrhaphies. 62% felt that they improved over all after surgery. Additional postoperative symptoms included: vaginal and/or perineal splinting (33%), soiling and/or inability to wipe clean (16%), rectal digitation (23%), incontinence of flatus (19%), and rectal and/or vaginal pain (22%). Thirty-three women (24%) had large rectoceles, seven of whom did not have impaired bowel emptying. Over half of the women were postmenopausal at the time of surgery and less than one-third were on hormone replacement therapy at follow up. Finally, most had had other vaginal or bladder neck surgery.

Silva (2006) evaluated 110 patients with advanced symptomatic uterovaginal or post-hysterectomy prolapse for issues relating to post operative sexual dysfunction. The mean follow-up period was 5.1 years (range 3.5-7.5 years). Vaginal hysterectomy (37.5%), anterior colporrhaphy (58.3%), posterior colporrhaphy (87.5%), and suburethral slings (31.9%) were performed as indicated. Surgical failure (symptomatic recurrent prolapse of stage 2 or greater in one or more segments) was 11 of 72 (15.3%). Two patients (2.8%) had recurrence of apical prolapse of stage 2 or greater. For those sexually active preoperatively and postoperatively (n=34), mean postoperative FSFI scores for arousal, lubrication, orgasm, satisfaction, and pain were normal, whereas the desire score was abnormal (mean = 3.2). However, 94% (n=29) were currently satisfied

with their sexual activity. Postoperative IIQ/UDI scores were significantly improved in all three domains (irritative, P=.01; obstructive, P<.001 stress, P=.03) and overall (IIQ-7, P<.OOl; UDI, P<.OOl) compared with preoperatively. Bowel dysfunction occurred 33.3% preoperatively compared with 27.8% postoperatively (P=.24). The authors concluded that uterosacral ligament vaginal vault fixation seems to be a durable procedure for vaginal repair of enterocele and vaginal vault prolapse. Lower urinary tract, bowel, and sexual function may be maintained or improved.

Lowman (2008) evaluated Prolift cases performed between August 2005 and August 2007 to determine the rate of de novo dyspareunia. Type and degree of dyspareunia were assessed by self-administered questionnaire. Demographics, use of hormone therapy, failure rate, and willingness to have the surgery again were summarized using descriptive statistics. Results indicated that the rate of de novo dyspareunia was 16.7%. Over 75% of patients with de novo dyspareunia described the pain as mild or moderate. Most described dyspareunia during insertion. 88% of the respondents with de novo dyspareunia would have the procedure done again. The authors concluded that Prolift is associated with a 17% de novo dyspareunia rate and despite this, most would have the surgery done again.

Dietz (2013) performed a Cochrane database review regarding the impact of prolapse surgery on sexual function. They found that with regard to the anterior compartment, the use of mesh is associated with neither a worsening in sexual function nor an increase in de novo dyspareunia compared with traditional anterior colporrhaphy (grade B). There is insufficient information to provide evidence-based recommendations on sexual function after vaginal mesh in the posterior compartment or after new

lightweight or absorbable meshes (grade D). The authors concluded that there is a paucity of data on the impact of prolapse surgery on sexual function. Sexual function and dyspareunia rates are similar after anterior polypropylene mesh and anterior colporrhaphy (grade B). They suggested the use of validated questionnaires measuring sexual function in women before and after prolapse surgery and reporting sexual activity and dyspareunia rates pre- and post-intervention in all patients.

Karram (2013) reviewed the safety and efficacy of surgery for posterior vaginal wall prolapse. This Cochrane database meta-analysis reviewed literature published up to 2012. They noted that higher dyspareunia rates are reported when levatorplasty is employed (grade C). Further, the transvaginal approach is superior to the transanal approach for repair of posterior wall prolapse (grade A). They noted that no studies have shown any benefit of mesh overlay or augmentation of a suture repair for posterior vaginal wall prolapse (grade B). It is for that reason why I have stopped using any graft augmentation for posterior repairs after 2012.

Damoiseaux (2015) sought to compare the long term effectiveness of trocar guided mesh with conventional vaginal repair in patients with recurrent pelvic organ prolapse (POP). Patients were randomized to either trocar-guided Prolift polypropylene mesh or conventional vaginal prolapse repair. Patients were followed for 7 years. Of the original 194 allocated patients, 135 (70%) were available for analysis.
There were no differences in baseline characteristics. POPQ stages, number of previous POP surgeries and number of previous treated compartments were equal between both groups. The composite outcome showed no difference in success rate between trocar guided mesh or conventional surgery using native tissues. The overall anatomic success

was higher in the mesh group, which was particularly significant for the anterior compartment (74 % vs. 31 %, p 0.001). The authors concluded that at 7 years follow-up the composite success rate of trocar-guided mesh insertion appeared to be equal to native tissue repair in this group of patients with a history of recurrent POP. Although the mesh exposure rate was higher than what is typically reported, the authors found no difference in pain rate or dyspareunia between the two groups.

Position Statements Regarding Prolapse Mesh Repairs

The American Urogynecologic Society (AUGS 2013) strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders. The AUGS statements are as follows:

1. A complete restriction on the use of surgical mesh was not the stated intent of the FDA safety communication.
2. The decision on surgical alternatives should be made by the patient and her surgeon.
3. A ban on surgical mesh would prohibit the surgical studies mandated by the FDA and recommended by the NIH, ACOG, and AUGS.
4. In some circumstances transvaginal mesh for pelvic organ prolapse may be the most appropriate surgical option
5. Any restriction of mesh slings for the treatment of stress urinary incontinence is clearly not supported by any professional organization or the FDA.

6. Any restriction of mesh placed abdominally for the treatment of prolapse is clearly not supported by any professional organization or the FDA.

7. Instead of a ban on mesh we recommend the implementation of credentialing guidelines so that mesh procedures are performed by qualified surgeons.

American College of Obstetrics and Gynecologists (ACOG) 2010 Statement notes that the risks of pain including pelvic pain, groin pain and dyspareunia can occur after any prolapse surgery. The only unique complication related to the use of vaginally placed mesh is erosion, exposure or extrusion. Vaginal "mesh repair should be reserved for high-risk individuals in whom the benefit of mesh placement may justify the risk, such as individuals with recurrent prolapse (particularly of the anterior compartment) or with medical comorbidities that preclude more invasive and lengthier open and endoscopic procedures." (ACOG CO #53, 2010). This is yet another example as to how pelvic floor surgeons should be aware that pelvic pain, groin pain, and dyspareunia are commonly known potential complications after any pelvic floor repair surgery.

The American Urological Association (AUA 2011) released a position statement regarding vaginal mesh for the repair of POP. They suggest that non-absorbable synthetic mesh may improve anatomic outcomes of anterior vaginal wall repair but there are significant trade-offs in regard to the risk of adverse events. Potential risks include chronic pain, dyspareunia, fistula, infection, and delayed graft erosion/exposure. Notably, many of these risks exist with alternative prolapse repairs and while mesh exposure is unique, suture erosion can occur with native tissue repairs and

exposure/erosion and wound granulation can occur with both synthetic and non-synthetic/biologic graft materials.

I agree with the discussion and conclusions in the Time to Rethink (2011) article written in response to the 2011 FDA Public Health Notification, including but not limited to the following:

- "This statement suggests that at least 225,000 TVM procedures are done in a 3-year period. In the 3-year period that this update addresses, there were "1,503 reports associated with POP repairs." Using these numbers the incidence of these reported complications is 0.67% (and the incidence may be even lower for TVM given that the news release states that "the reports don't always differentiate between transvaginal and abdominal procedures")."
- "Since no FDA-monitored device is used in this and other native tissue repairs, it is difficult to know how many similar complications would be reported to the FDA if an alternative reporting mechanism were in place. Thus the assertion stated as the purpose of the UPDATE that TVM "may expose patients to greater risk" than traditional nonmesh repairs is unsupported."
- "In the TVM review, the rates vary from 0% to 29.7%. In fact, in one multicenter RCT of TVM, the rate of erosion between sites ranged from 0% to 100% [5], Since the same mesh and delivery system were used in similar patient populations, it is reasonable to conclude that this variation is not a function of the mesh itself but rather the surgical technique."
- "Mesh complications are not the only complication patients are at risk for when undergoing surgical repair of POP. The risk of complications involving the

abdominal wall (i.e., incisional hernia) and small bowel is almost certainly higher with ASC since the peritoneal cavity is traditionally not entered with TVM. Secondary analysis of one large RCT of ASC [6] concluded that one in 20 women experiences significant gastrointestinal morbidity after ASC. More than half of most mesh exposures from TVM are asymptomatic, and one third need only minor outpatient operative intervention [5]. However, a small bowel obstruction following an open abdominal sacral colpopexy may require a second laparotomy and a prolonged inpatient admission. Thus while the rates of "complication" may be higher with TVM, the severity of the complications associated with ASC may be greater."

- "We therefore agree with the portion of the UPDATE that states, "mesh augmentation may provide an anatomic benefit compared to traditional POP repair without mesh"—but we find the statement "this anatomic benefit may not result in better symptomatic results" highly questionable. Given the current data, it would be equally true to state that "this anatomical benefit may result in better symptomatic results."
- "The UPDATE refers to mesh contraction (shrinkage) as a previously unidentified risk of TVM. While contraction may occur in some cases, analysis of translabial four-dimensional ultrasounds of 40 patients who underwent anterior mesh procedures showed no evidence of mesh contraction between their first and last postoperative visits [21], This is only one imaging study, and the results have not yet been duplicated; however, we do have comparative clinical data. All but one [15] of the eight RCTs of TVM [5, 11—14, 16-19] measured pre- and

postoperative vaginal length. None of these studies showed any difference in the change in vaginal length after surgery between the mesh and nonmesh arms of the studies. If there is shrinkage with TVM, it does not appear to affect vaginal length any more than does the trimming of the vaginal wall during standard colporrhaphy with native tissue."

- "In regards to pain with intercourse, one of the eight studies did not assess sexual function [16], but the remaining seven did. In one study, the dyspareunia score was significantly worse in the no mesh group at 2 years out [14]. In the others, no difference in sexual function was noted between the TVM and traditional repair groups [5, 12, 13, 15, 17-19]."
- "Studies show that traditional POP repairs can have high rates of failure [22, 23], Factors such as patient age and severity of prolapse [24] can affect the chance of prolapse recurrence and should be taken into account when counseling patients. We agree that POP can be successfully treated without mesh in many cases, but not necessarily most. At the very least, a statement clarifying that success in treating anterior compartment and recurrent prolapse may be more likely with the use of mesh would lend balance to the FDA's communication."
- "We also feel that the remainder of the recommendations (i.e., "Inform patients about the potential for serious complications and their effect on quality of life, including pain during sexual intercourse...") applies to nonmesh POP repairs as well."
- "The fundamental flaw in the FDA's analysis is that it is based on the question of proof of superiority of mesh in all patients. No one is suggesting that mesh is

recommended for all patients. However, there may be instances when a surgeon suspects that a native tissue repair will have a high risk of failure and that the potential benefits of a mesh repair outweigh the risks. The purpose of this response is to demonstrate that TVM is an important tool in our surgical armamentarium that may be the best option in some cases. From our vantage point, it appears that the FDA has presented a biased view of TVM among all POP repair procedures because of the current reporting mechanisms in place."

Prolift IFU

The first Prolift IFU was released in 2005. The IFU is intended for pelvic floor surgeons who are "familiar with surgical procedures and techniques involving pelvic floor repair and nonabsorbable meshes." Although Ethicon was not required to provide professional education, Ethicon made training available to surgeons, and Ethicon's Prolift IFU stated that training on the use of Prolift "is recommended and available." Ethicon's IFU also refers surgeons to the surgical technique guide. The Prolift IFU has clear indications that the system was indicated for tissue reinforcement and long-standing stabilization of fascial structures of the pelvic floor in vaginal wall prolapse. This can be used for mechanical support or bridging material for the fascial defect. It is appropriately assumed that the surgeon who is going to perform this procedure has ample experience with POP procedures and understands pelvic floor anatomy. The pictures of the mesh implants, Prolift Guide, Prolift Cannula and Gynecare Retrieval Device are accurate. The pictorals in the IFU clearly state that they are not intended to provide any clinical teaching but are to only demonstrate the general use of each device. This is certainly fair

to assume given surgeons skills and training. The contraindications stated for the device are appropriate as this mesh should not be used in infants, children, pregnant women or women who are planning future pregnancies. The warnings and precautions are clearly stated. Users of Prolift should be familiar with surgical procedures and techniques of the pelvic floor and nonabsorbable meshes before they consider employing the Prolift procedures. The IFU clearly states that acceptable surgical practices should be followed in the presence of infected or contaminated wounds. The recommendations to refrain from intercourse and heavy lifting/exercise until cleared by their physician is standard for all pelvic floor surgical procedures.

The IFU clearly states that the physician should avoid placing excessive tension on the mesh implant during handling. It is up to surgeon's judgment to exercise the tension-free adjustment, similar to how a surgeon performing an autologous fascial sling would have to use surgical judgment to place the sling tension-free. Any excess tension on the mesh arm is generally handled with ease by performing a release procedure and without having to remove the mesh. This is particularly important as many believe that such tension is the cause of adverse events seen in the post-operative course. Further information on this important concept are discussed in the Ethicon Professional Education materials. Tension-free mesh placement is of great importance and is easily learned. There are several guidelines to keep in mind that are discussed in the monograph. First, there is no need to overpull on the mesh wings and this can be done under vision. Second, the mesh is to be placed loosely because this allows maintenance of vaginal length and caliber during the healing phase. Third, it is important during

posterior graft adjustments to perform a rectal examination to make sure there is no evidence of rectal injury.

Additionally, the IFU clearly states that the system should be used with care to avoid damage to vessels, nerves, bladder and bowel. Attention to patient anatomy and correct use of the device is stressed in the IFU. The IFU describes the warning of transient leg pain.

With regard to adverse reactions, the IFU clearly describes the commonly known adverse reactions that are specific to the device, and discusses the complications that can result in symptoms of pain and dyspareunia (which were later added to the Prolift IFU in 2009).. The IFU discusses important adverse reactions including infection potentiation, inflammation, adhesion formation, erosion, extrusion and scarring that results in implant contraction. While the 2005-2009 Prolift IFUs do not specifically mention pain and dyspareunia, the IFU is still adequate because these complications, including their frequency and severity, are well-known to all surgeons who perform pelvic floor surgeries regardless of whether or not mesh is used. Further, the abovementioned complications, when present, will often present with pelvic pain and dyspareunia. Thus, any physician who performs this procedure who has reviewed the IFU will not only appreciate the importance of these complications, but will realize that they can present with pelvic pain and/or dyspareunia post operatively and look to elicit such complaints at post operative visits and during interval pelvic examinations. Finally, the IFU clearly states that punctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during the procedure and may require surgical repair. This certainly urges surgeons to appreciate the complexity of the procedure and to follow the procedure steps

carefully and make sure they are familiar with surgical procedures of the pelvic floor, nonabsorbable mesh and the relevant anatomy. Additionally, it is well-known that patients with pelvic organ prolapse can have impaired sexual function due to the anatomic deformity in the patient with cystocele and/or rectocele. Reducing the bulge present with the Prolift procedure, sexual function can certainly be restored. Thus, it is certainly possible that normal sexual function can result from treatment of POP. The IFUs are adequate from a clinical standpoint as well as a regulatory standpoint, per 21 CFR 801.109(c), which permits manufacturers to omit warning information that would be commonly known to practitioners licensed by law to use the device.

The Prolift IFU was revised in 2009. Some of these additions included information that is obvious to physicians who perform pelvic floor surgery such as the performance of a DRE to detect possible rectal perforation and that cystoscopy may be performed to confirm bladder and ureteral integrity. The 2005 IFU already mentioned the possibility of rectal or bladder injuries so the mention of DRE and cystoscopy in the 2009 IFU is, in my opinion, unnecessary. Further, the 2009 IFU mentions that the device should not be used in the presence of active or latent infections or cancers of the vagina, cervix or uterus. These additional statements are similarly unnecessary as pelvic reconstruction in the setting of active infection or gynecologic cancer is strongly discouraged. The 2009 IFU also mentions that potential adverse reactions are those typically associated with pelvic organ prolapse repair procedures (referring to mesh and non mesh procedures), including pelvic pain, pain with intercourse. These may resolve with time. This statement, as well, is assumed to be true for all pelvic surgeries and in my opinion is assumed to be known by all physicians who perform pelvic floor

surgeries. These are commonly known potential complications of any pelvic floor repair surgery. Another revision to the Prolift IFU included a section entitled Clinical Performance. This section included randomized controlled clinical evaluations including 12-month post marketing data. Adverse event data was reported including hematoma of 3.5-4.5%, abscess 0-1.1%, UTI within 6 weeks of the procedure 8.2-16.9%, mesh exposure 10-14%, surgical intervention for mesh exposure 5.6-7%, vesicovaginal fistula 1.1-1.2%, rectovaginal fistula 0-1.1%, moderate to severe mesh retraction 3.6-12.6%. These complications have been replicated in other studies and shows the manufacturers diligence in providing this information to surgeons.

Prolift Patient Brochure

The first Prolift Patient Brochure (2005) entitled Get the Facts, Be Informed, Make YOUR Best Decision was a full-color, 16 page guide for patients. This easy to read document provides patients information on pelvic organ prolapse, its common symptoms, the different types of pelvic prolapse as well as a brief discussion of treatment options. A relevant discussion of Prolift is provided with basic information about how it differs from other surgical procedures and how it works. A discussion of the mesh being held in place initially by friction created by the strap like arms of the mesh and then the body ingrowth into the mesh pores creating the final support. This is a realistic discussion of the basic goal of the Prolift procedures and is appropriate for inclusion in this brochure. A discussion of the risks of the procedure are discussed which mentions injury to blood vessels of the pelvis, nerve damage, difficulty urinating, bowel and bladder injury. There is also mention of the small risk of mesh material becoming

exposed into the vaginal canal. The risks mentioned imply that if any of the above problems occur that patients will experience pelvic pain and dyspareunia. It is not necessary that they be included in this pamphlet as it is quite obvious that if mesh is exposed in the vaginal canal that pain and dyspareunia can result. The brochure makes no attempt to create a standard patient that should undergo a Prolift procedure. It mentions clearly that only a complete physical examination and consultation with a physician can determine the appropriate procedure for a patient.

The Prolene mesh is soft and is pliable when placed correctly so that issues with erosion or extrusion would be reduced and unlikely to occur. However, patient characteristics play role in how the mesh is incorporated into the tissue. It is well-known that patients over the age of 70, those that have a more significant degree of prolapse, or are current smokers, will have increased rates of scarring, mesh contracture, erosion or extrusion. Further, vaginal healing and perivaginal blood flow in such patients is likely impaired and further contributes to these issues. It is the surgeon who must make the clinical decision based on the history, physical examination and desires of the patient as to whether Prolift is right for them.

The final page of the brochure provides information about the indications of the procedure which include tissue reinforcement and long lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended, either as mechanical support or bridging material in the fascial defect. Physician warnings and precautions are also mentioned which include that the users (physicians) should be familiar with surgical procedures and techniques involving pelvic floor repair and non-absorbable meshes before employing the Prolift Repair

System. Thus, this empowers the patient to ask their physician if they are comfortable with performing this procedure, how many they have performed, their success rates, and their complications they have encountered. It furthers the position that the ultimate responsibility with this procedure will fall on the physician who is performing it. Additional discussion about avoidance of placing tension on the mesh implant during handling is mentioned as well as the risk of damage to vessels, nerves, bladder and bowel as well as the requirement of the physician to be attentive to patient anatomy and correct use of the device to minimize risks. This additionally furthers the suggestion that the ultimate responsibility for success with this procedure falls on the physician.

A discussion of pertinent adverse reactions are included which are associated with surgically implantable materials, including infection potentiation, inflammation, adhesion formation, fistula formation, erosion and scarring that results in implant contraction. Pelvic pain and dyspareunia are not mentioned here but it is obvious that any patient who has the abovementioned symptoms will experience pelvic pain and/or dyspareunia. Thus, those entities do not need to be mentioned specifically in the Patient Brochure.

Additional versions of the Prolift Patient Brochure were released in subsequent years with additional information as it came available and included a more in depth discussion of the commonly known potential risks. For example, in the 2008 Patient Brochure, Ethicon included the following information: "All surgical procedures present some risks. Complications associated with the procedure include injury to blood vessels of the pelvis, difficulty urinating, pain, scarring, pain with intercourse, bladder and bowel injury. There is also a risk of the mesh material becoming exposed into the vaginal canal.

Mesh exposure can be associated with pain during intercourse for the patient and her partner. Exposure may require treatment, such as vaginal medication or removal of the exposed mesh. Synthetic mesh is a permanent medical device implant. Therefore, you should carefully discuss the decision to have surgery with your doctor and understand the benefits and risks of mesh implant surgery before deciding how to treat your condition."

However, the initial Patient Brochure described above (2005) was still sufficient in depth and breadth to accurately describe Prolift to patients and portrayed risks in a realistic manner, as well as serving as a tool to facilitate the physician-patient discussion. By no means should a Patient Brochure replace the counseling process, nor is a Patient Brochure designed or intended to do so.

Prolift Professional Education Physician Video (2005)

The video initially illustrates the purpose of hydrodissection. This maneuver is twofold. First, it facilitates surgical entry into the true vesicovaginal space and facilitates full dissection into the lateral pelvic sidewalls and back to the initial spines. Second, its goal is to provide hemostasis. Hydrodissection is not a unique maneuver utilized for the Prolift procedure. It can be used to facilitate dissection for any pelvic floor procedure such as, but not limited to anterior repair, posterior repair, urethral diverticulum repair and urethrolysis.

There is a clear description with illustration of the concept of trocar passage. With regard to trocar passage during the Prolift Procedure, this is not a blind passage of the trocar. When placing the trocar with its guide, the surgeon's finger should be positioned in the paravaginal space against the obturator internus muscle near the

pubic arch in order to meet the instrument. In this manner, there is very little tissue between the trocar and the surgeon's finger allowing for safe passage. Since the vaginal dissection is complete at this point, any untoward bleeding can be seen easily. Further, the bladder is also well dissected and can be displaced so as to avoid inadvertent bladder injury. In my personal experience, I have never had a bladder injury nor a vascular injury from trocar passage. Additional trocars are placed under finger guidance posteriorly and in total 4 passes are undertaken regarding the trocars for the anterior repair. With regard to placement of the straps near the pubic arch and ischial spine on each side, the body of the implant is able to be placed along the arcus tendineus fascia pelvis of the pelvic sidewall. This does recreate the support of the pubocervical fascia underneath the bladder from sidewall to sidewall.

With regard to the straps of the mesh, these straps are adjusted as the implant is pulled up into the vesico-vaginal space under the bladder. In this DVD there is no discussion of tensioning in any way. Tensioning is not the appropriate word as we are actually attempting to carefully "position" the mesh along the course of the pubocervical fascia from arcus tendineous to arcus tendineous bilaterally. This point is well illustrated in the video.

The Prolift Procedure Video (2005) clearly describes and illustrates the concept of mesh placement without tension. The mesh must be placed to cover the prolapsed space from arcus tendineous to arcus tendineous bilaterally along the course of the pubocervical fascia. This is not done with any tension and this is determined by the surgeon's finger in the vagina reassured the surgeon of accurate mesh placement. Further, with the finger positioned in the vagina, the completeness of dissection and identification of the bladder

helps to ensure that the trocar followed the proper path and to significantly reduce the chance of injuring the bladder.

CD disclaimer. The CD ROM was developed and provided for as an educational service with information regarding Gynecare Prolift. The content is intended to be used for education but is not a substitute for professional education, training or expertise. The disclaimer stresses that adequate familiarity with the use of the device in these procedures must be professionally acquired prior to use.

Prolift Physician Education Slide Presentation Deck (2005)

As part of training to use the Gynecare Prolift, Ethicon developed several Professional Education materials, including powerpoint presentations. The slide decks were used in the didactic portion of Ethicon's Professional Education programs. The slide decks provided additional material for surgeons to better understand the rationale for the use of mesh compared to native tissue procedures, to better understand the surgical technique, to better appreciate the anatomic landmarks, and to become more familiar with the success and complications reported in the medical literature.

The 2005 Prolift slide deck provided important information regarding mesh selection criteria. For non-potentiation of infection, the use of monofilament knitted mesh with a pore size greater than 75 µ and interstices > 10 microns are utilized. This allows for angiogenesis and ingrowth of fibroblasts and collagen. To maximize sexual function the use of soft flexible material is utilized. The slide deck includes data from Nygaard (2004) showing an erosion rate for polypropylene of less

than 1%. This paper also highlighted the erosion rates of material such as Marlex, Teflon, Mersilene and Gore-Tex with erosion rates between 3 and 5%.

The slide deck clearly defines mesh exposure in terms of mesh extrusion versus mesh erosion. Mesh extrusion typically occurs in the short-term. In this instance, the wound does not close around the mesh, similar to a wound complication after a native tissue repair.

The slide deck describes the study by Achtari (2003) which is a review of 198 POP patients who had a prolapse repair reinforced with mesh. The authors noted that mesh exposure decreased from 19% to 4% over the 3 year trial with the same surgeon. This information is important and highlights the same success that I have achieved during my experience with Prolift. My mesh exposure cases came early in my experience and were associated with larger degrees of preoperative prolapse. Thus, there is a surgical technique and experience component to reducing complications which cannot simply be blamed on the mesh being "defective."

The slide deck described the Transvaginal Mesh group (TVM) which, was created and developed by 9 French physicians. The primary objective was to develop a standardized procedure, which would be easy to conceptualize and to perform. Additional objectives include the opportunity to understand the mechanism of POP as much as possible and to reduce mesh exposures associated with POP surgery.

A discussion regarding mesh and vaginal reconstructive surgery regarding fixation was undertaken in the slide deck. The concept of suturing mesh to the ligament is more resistant to displacement and this is important because of difficult vaginal access to structures like the arcus tendineus fascia pelvis and also risk of contraction and

shearing. This is well described by Ethicon in the slide deck noting its importance even at the launch of Prolift. Discussion regarding the free arms placed in dissected spaces is important. It is mentioned that dissection is technically less difficult and inadequate resistance of the arms leads to displacement. It is suggested that larger size meshes should be used rather than smaller sizes. The mesh should be suspended both apically and laterally and that the use of tension free arms is preferred to the use of sutures.

The slide deck highlights an important study with significant patient enrollment. The TVM group undertook a retrospective study from January 2002 to December 2003 evaluating 277 patients using polypropylene soft mesh and polypropylene mesh. The authors noted intraoperative complications including rectal injury in one patient (0.36%), bladder injury in 3 patients (1.4%), hemorrhage or hematoma in 10 patients (3.6%). Intervention was required in 2.8% of patients and these were due to dissections and not due to the mesh. Postoperative complications included vaginal adhesions in 10 patients (3.6%), symptomatic tissue contraction in 4 patients (1.8%), vaginal exposure with mesh in 25 patients (9.2%). All of these complications were felt to be related to the mesh. The anatomic failure rate at 1 year occurred in 11 patients (4%). Of note is that Ethicon has warned physicians through their professional education material of the known complications that could occur with Prolift. Further, it is mentioned that uterine conservation was associated with decreased mesh exposure rate. For patients with a hysterectomy, mesh exposures occurred in 24 patients (14.6%) whereas in those patients without hysterectomy, mesh exposures occurred in 1 patient (0.9%). This is important information for Prolift implanters to understand as they began to use this product. Further information about incision

technique for Prolift was provided in this study. When the 25 anterior TVM erosions were evaluated by incision type, The T incision resulted in 21 exposures (16.7%), the paracervical incision resulted in 3 exposures (7.9%) while the longitudinal incision resulted in 1 exposure (0.9%). It is for this reason that Ethicon recommended that surgeons utilize the longitudinal incision as it had the lowest mesh exposure rate. With regard to the defect type and implant exposure rate, the TVM in the anterior compartment resulted in 33 patients with mesh exposure (14.4%) and 1 patient with mesh exposure in the posterior compartment (0.5%).

The TVM Experience learnings are very important concepts for physicians who plan to utilize Prolift and Ethicon shared this information with physicians. First, exposure rate requiring intervention is 9%. Exposures are more common in the anterior versus posterior compartment. Exposures are more common when a hysterectomy is performed as opposed no hysterectomy. Exposure was more common when the T-incision was used versus a longitudinal incision. Again, this information provided implanting surgeons with a great deal of information as to how to approach this procedure.

The slide deck provided extensive detail on the Gynecare Prolift system implants showing pictures of the anterior implant, the posterior implant and a total implant system. Instruments were also shown in pictoral form as well as a significant number of diagrams of the total implant and the proper procedure to place, remove, leave the cannula, pass and retrieve the device. Pictures were also provided illustrating the important neural and vascular structures showing important muscles such as the gluteus maximus muscle as well as the relationship to the trocar passage and important nerve

structures such as dorsal nerve of the clitoris, peroneal nerve, pudendal nerve, inferior rectal nerve, peroneal artery, Alcocks Canal and the inferior rectal artery are well visualized. One can see exactly where the needle guide is placed and how to avoid injury to these structures.

Prolift Physician Education Slide Deck (2007)

In 2007, Gynecare updated their physician education training for the Prolift procedure. A 90 slide physician education program was produced for physicians. This was made available to all physicians by Gynecare. The slides discuss the increasing prevalence of POP. The lifetime prevalence is approximately 30-50% with women over 65 as the fastest growing segment of the population. This will create an increase in POP surgeries performed. The presentation discusses possible causes of prolapse surgery failure. These include anatomic, tissue factors, environmental factors, as well as surgical factors. Causes of failure of POP repairs are discussed which include loss of tensile strength of the pelvic floor and failing to restore and maintain normal anatomic position and function. These causes of failure suggest the importance of performing a quality surgical repair.

The slide presentation describes the Amid classification of materials used for prolapse surgery. Type I is where pore size is greater than 75 µm. The component is polypropylene. The fiber type is monofilament. The trade name can include Prolene by Ethicon, Marlex by Bard, Atrium by Atrium and Gynemesh. Ethicon's TVT and Gynemesh PS meshes are both well over the 75 micron threshold and are considered Amid Type 1 large proe, light weight meshes.

The presentation describes biomaterials used in ASC. Nygaard (2004) published a long-term review of ASC. They reported a success rate of 78-100%. They noted poor outcomes with endogenous, donor fascia, and xenograft. They noted an overall mesh erosion rate of 3.4%. The slide deck addresses the possibility these softer meshes such as those with more porous polypropylene will result in lower erosion rates.

The strength and weaknesses of ASC are discussed. The same complications that can result from using mesh in an abdominal sacrocolpopexy repair are the same set of potential complications that can occur after a Gynemesh PS transvaginal or Prolift repair. Prior to Prolift, complications such as mesh erosion, mesh exposure, pain, dyspareunia, scarring, contraction, recurrence, etc., were commonly known and documented in the medical literature (Iglesia 1997, Cosson 2003). The weaknesses of this procedure are that general anesthesia are required. With an abdominal sacrolcolpopexy, the patient often stays in the hospital for several days and there is morbidity from the laparotomy portion. These morbidities can include pain, respiratory compromise, small bowel obstruction/ileus, thrombosis, and incisional hernia. The goals of Prolift surgery emulate the outcomes obtained with ASC, with lower morbidity, and improved patient experience. Vaginal implantation of mesh in a tension-free manner offers promise.

The design of the Prolift is discussed in the presentation. Pictures of the instruments are shown as well as diagrams of the pertinent anatomy for the anterior and posterior procedures. The principles of transvaginal mesh placement are described in the presentation.

Cosson's (2005) 9-center study with 687 patients is reviewed in the presentation. 25% had prior hysterectomy. This group noted an overall rate of

postoperative complications of 1.3%. These complications included rectal injury, bladder injury, hemorrhage, cellulitis, abscess, and hematoma. Also described are postoperative complications including mesh contraction in 3% of patients, de novo stress incontinence in 5% of patients, vesicovaginal fistula and rectal mesh exposure in a minority of patients. The overall mesh exposure rate was 13.4%. 7% of patients were treated expectantly while the remaining 7% required intervention in the operating room. This group also studied the type of incision that required intervention. Patients who had the "T" incision had a 16% chance of requiring intervention. It is for this reason the Ethicon recommended not using the T-incision.

Miller's (2006) research in the United States using transvaginal mesh was discussed in the presentation. 85 patients at 3 sites were studied all with six-month and one-year follow-up was also highlighted in the slide deck. Anatomic failure was noted in 12%. The mesh exposure rate over 12 months was 12.9%. Sexual activity and dyspareunia were also described. Preoperatively nearly 30% of patients noted that their sexual activity was limited by their prolapse. 39% patients preoperatively had dyspareunia. However, at one-year follow up only 2.4% of patients had dyspareunia. Ethicon makes clear that dyspareunia is a risk with the use of pelvic mesh in this presentation.

The presentation reviewed the Jacquetin (2006) paper which is a prospective multicenter trial. 175 patient's were studied with one-year follow up. 11 patients had mesh exposure. All of these patients required outpatient intervention. 2 urogenital fistulas were noted. Sexual function was studied extensively. The dyspareunia rate was 20% at baseline and improved to 3.9% at one year. The paper describes de novo dyspareunia in

3% of patients. Pelvic pain improved from 27% at baseline to 7% at one year. The group noted anatomic success of 85% at one year.

The guide and cannula system were discussed in the slide deck. This allows for palpation guided, anatomically accurate, controlled placement in all 6 sites with a single system. The six-site system is used for the total anterior and posterior repair. The cannula system allows the mesh arms to be placed and adjusted without tissue tearing. Pictures of the guide, cannula, retrieval device, total mesh implant, anterior mesh implant and posterior mesh implant are shown. High-quality pictures showing the external landmarks and incision sites are shown as well as pertinent neurovascular structures so that the physician will be well aware of these as the procedure is performed.

The presentation discussed hydrodissection. This step is critical to the performance of POP surgery and is recommended with 20-80 cc of hydrodissection fluid to be utilized. This allows the physician to get into the true vesicovaginal, or rectovaginal space. Tips to successfully perform this are given including avoiding bunching as well as estimation of the thickness with palpation, and the correct space of the path of least resistance. These are important facts for the physician using Prolift to know and it is well described in this Physician Education update.

Next, the presentation discusses the endopelvic fascia. The anterior compartment and posterior compartment are discussed. The slide deck mentions that there is no "true vaginal fascia." There is a description of surgical placement of mesh in the vaginal wall showing the true vaginal spaces and potential sites for graft placement. Of note, is this was described in 1994, well before Prolift came onto the market. Next, detailed description with pictures showing a full-thickness vaginal incision is shown. The slide

shows that the physician must identify the true vesicovaginal and rectovaginal spaces. The use of full thickness flaps can lower erosion rates. This is important for physicians to know, and is another example of how improved surgical technique can reduce complications. Next, a discussion of appropriate cannula placement is shown with excellent pictures. A discussion of the pertinent nerves, arteries and veins are shown so that the physician can effectively place these trocars. A detailed discussion of retrieval suture recovery is undertaken. The superficial anterior passes can be done visually without problem. The deep anterior sutures can be identified with or without visualization. The slide deck clearly shows that for visualization, the use of a long retractor assists with this step. Without visualization one can use the hand held cannula between the index and middle finger.

Mesh implantation is described in detail in the slide presentation. Color graphics are shown showing the mesh lying flat in the vaginal space. Details on how to close the colpotomy are given. The consensus is that a simple running suture is appropriate and there is no need to trim the vaginal wall. A discussion of mesh adjustments is undertaken. The mesh should be loosely applied. It cannot be "too loose." The vagina is closed and is restored before the final adjustments to the mesh position are made. Detailed anatomic pictures of the posterior system implant, the appropriate anatomic landmarks, dissection, and anchoring are clearly shown in the slide deck. There is a section with excellent graphics of the total system implant as well as showing pertinent external landmarks an incision sites, as well as the pertinent anatomy.

A careful discussion about postoperative care is undertaken. Packing is left in for 24-48 hours. Antibiotics are given for one dose preoperatively and additional doses

within the first 24 hours. Pain management, stool softeners and hospital stay are described. Of importance is follow up for patients receiving Prolift. Follow up is recommended at 2 weeks, 6 weeks, 3 months, 6 months, 12 months, and annually thereafter.

The slides review Davila's (2006) discussion about patient's selection. Previous failures, primary repair in severe defects, older sexually inactive patients, and patients at high risk for failure, are discussed. Relative contraindications are also described which include previous radiation, immunosuppression, severe urogenital atrophy, active infection, and the role of host factors. This is a very important section because these are patients who are likely to have early recurrence including patient derived factors. These include: systemic corticosteroids, poorly controlled diabetes, heavy smokers, and morbid obesity. A discussion of the importance of cystoscopy was provided. Cystoscopy is certainly recommended with Prolift.

The slide set notes that there is a risk of cystotomy. In these procedures it is approximately 1-2%. General cystoscopy guidelines are given. Specifically any difficulty encountered during the Prolift procedure, after cannula placement and before mesh delivery, and after completion of the procedure to evaluate the ureter and bladder are good reasons to consider cystoscopy. This is well described by the manufacturer. A discussion about dividing the mesh and trimming the mesh is also undertaken. Mesh trimming is common. Shortening the posterior flap occurs in the majority of cases. Minor anterior and distal length adjustments are also common. There is no consensus for dividing the mesh in a total Prolift repair. There is opinion that splitting the piece of mesh

may result in future dyspareunia. The fact that this is mentioned in the slides set is important because it shows physicians that this is a real risk.

The presentation talks about the concomitant use of the Gynecare TVT at the same time of prolapse repair. A discussion of prophylactic treatment of occult SUI is provided for physicians. Three approaches are suggested. First, is a sling for a patient with a positive pessary test or urodynamic evidence of occult SUI should be considered. Second, the de novo SUI can be treated at a separate setting, in an additional surgery. Third, slings can be placed in all patients with urethral hypermobility. It is important to note that this information is included in the slide set so that physicians can decide which procedures to perform and when.

Next discussion about healing abnormalities after the procedure are discussed. The exposure rate experience is variable. There is a range of 1-8%. Most exposures of mesh occurred at the incision line anteriorly. A discussion of how to manage exposures discussed. Early exposure (< 4-8 weeks) of the mesh discussed. Early exposure mesh is often managed conservatively with topical estrogen. Late exposure, greater than 4 weeks after surgery is discussed. If there is large area of mesh exposed this is often managed operatively. Tips are suggested. First is to prevent mesh redundancy. Second is not to use tension. Third is not to incorporate mesh into the closure.

A discussion of bleeding is then undertaken. The slides discussed packing the affected side and continuing the procedure. It is described that the fastest way to stop venous bleeding is to apply direct pressure and then finish the procedure. Tamponade with packing is often helpful as well. Suggestions for dealing with refractory bleeding include placing advanced hemostatic agents on the prolapse, and selective arterial

embolization. Visceral injury is also discussed. The procedure should be aborted when obvious rectal injury has occurred. Controversy exists regarding mesh implantation after cystotomy. Fistula formation after surgery has also been reported. It is important that Ethicon provided this information to surgeons to augment their current learning of these complications. Dyspareunia is also discussed in the slides. To avoid pain, the procedure must be tension-free. Rectal pressure can occur for up to 8 weeks after the procedure. Persistent rectal pain can be attributed to tight posterior straps. Treatment options include physical therapy, local anesthesia, steroid injection, strap division, resection, mesh removal.

A discussion of early outcome data is described in the slide deck. Eight studies are described in the slide deck with data on approximately 550 patients. The mean age is 64 years. 50% patients underwent a total anterior and posterior repair. Cystotomy occurred in 1.7% patients. Rectal perforation occurred in 0.4% patients while bleeding was noted in 1.3% patients and voiding dysfunction in 6.7% patients. Mesh exposure was noted in 6.2% patients. The length of follow up is 6 months. Success as defined by a less than stage II POP is 81-100%. Data from Fatton (2006) and Murphy (2006) reported on sexual function in patients undergoing Prolift. Approximately 180 patients were studied with follow up between 5 and 12 months. Postoperative sexual pain occurs in approximately 5-8% of patients.

Prolift Surgeons Resource Monograph (2007)

In 2007, Ethicon produced a Surgeons Resource Monograph. This 41 page document was created to provide surgeons with expert opinions on the use of the Gynecare Prolift System including total, anterior, and posterior repair systems.

A section on patient selection is provided. This procedure is useful in any patient that a surgeon feels would require synthetic graft augmentation. Only the treating surgeon can determine where it is best used, although in patients with previous failure, patients with risk factors for failure, and/or the most severe degree of prolapse, Prolift has been successfully employed and has the clearest indications. It is a procedure of low invasiveness that ideally can be performed in less than 2 hours. The Prolift procedure is best utilized in patients with appropriate medical conditions, but surgeons should exercise caution in patients in either extreme age or are in poor health. The guide points out that there are no absolute age restrictions. A well estrogenized vaginal wall is certainly preferred and a poorly vascularized vaginal wall can also be considered for Prolift as long as careful postoperative follow up is undertaken. The guide points out that even when vaginal erosions occur in the post operative period, with appropriate treatment, the patient will generally do well despite this event.

The consensus of attendees at the Gynecare Prolift System Users forum has been that the rate of dyspareunia is low. Many surgeons have found that Prolift has lower rates of dyspareunia than some historical procedures such as posterior repair. The available early data on Prolift supports this notion. Nonetheless, data on impact of this procedure on sexual function is still being collected and evaluated.

A detailed discussion of surgical technique, anesthesia and hydrodissection, as well as incisions of choice are described in this monograph. Emphasis was placed on

patient positioning so that the correct insertion of the cannula can be completed. This is also critical for prevention of nerve injury and limiting postoperative pain. The importance of bony landmark palpation is discussed. The importance of lower extremity sequential compression devices during positioning is advised especially for patients with known risk factors for DVT formation. As for anesthesia, the choice is up to the surgeon and the anesthesiologist. The importance of hydrodissection cannot be understated. This was discussed in great detail in this monograph. Next, a detailed discussion of incisions is undertaken. The chosen incision should avoid the erosion prone apex.

A discussion of uterine conservation is undertaken. This remains controversial and the literature is not able to provide definitive answers. Some technique pearls are provided for the patient who had a prior hysterectomy or if uterine conservation is being considered. A discussion of mesh handling is undertaken. The lightweight macroporous monofilament polypropylene has been shown to be the best tolerated mesh available to clinicians today. The monograph discusses the concept of mesh contraction. An estimated 10-20% mesh contraction may be noted and this is why the monograph suggests that it is important to avoid excessive mesh trimming intraoperatively.

A discussion of technical pearls is then undertaken. The cannula and retrieval device are well engineered devices. The primary purpose of the cannula is to prevent linear tearing in the muscle which it passes through. The cannula should be handled with that in mind and kept stationary to avoid displacement. The trocar was designed to allow surgeon to pass the mesh through the sacrospinous ligament with ease. This is not a blind procedure. This can be done under vision to guide the retrieval device to the introitus by the use of Briesky retractors and forceps. Tension-free mesh placement is of great

importance and is easily learned. There are several guidelines to keep in mind that are discussed in the monograph. First, there is no need to overpull on the mesh wings and this can be done under vision. Second, the mesh is to be placed loosely because this allows maintenance of vaginal length and caliber during the healing phase. Third, it is important during posterior graft adjustments to perform a rectal examination to make sure there is no evidence of rectal injury.

The monograph discusses the postoperative care and complications of the Prolift procedure. Intraoperative complications including hemorrhage, visceral injury, and ureteral obstruction. Postoperative complications include hemorrhage, hematoma, fistula, infection, urinary retention, mesh exposure, mesh erosion, dyspareunia, and vaginal pain. With regard to bleeding, this is usually a direct consequence of trocar placement. When the correct plane is entered there is often very little bleeding. On the other hand, placing a trocar in the incorrect plane can be associated with significant bleeding. Strategies for dealing with bleeding intraoperatively are discussed in detail in this monograph. With regard to visceral injury, any occurrence of an intraoperative rectal injury, simple repair can be undertaken with multi-layer closure. Many suggest that the placement of mesh after a bladder injury has been reported and surgeons have performed a watertight multilayered closure and it proceeded with placement of the mesh without complication. Ureteral injuries were also discussed and they have been encountered in the patient with advanced prolapse who has tortuous and displaced ureters. It is for this reason that a cystoscopy with visualization of urine coming from both ureters should be undertaken during the Prolift procedure.

The complications of mesh erosion, exposure and extrusion are described and discussed in detail. The known recurrence of simple vaginal mesh exposure occurs in 17% of patients. Surgeon experience and avoiding hysterectomy when possible will reduce the rate to approximately 6%. Mesh exposures can spontaneously resolve early on but is less likely after an extended period of time. Many exposures are asymptomatic and require no treatment. The monograph discusses that these may become symptomatic over time. Symptoms can include dyspareunia and/or vaginal pain. Strategies for the treatment of mesh exposure are provided in the monograph. Further, the monograph provides suggestions for the prevention of this complication. The best prevention is strict adherence to the surgical technique guidelines with full-thickness incision, proper tissue handling, no vaginal trimming, tension-free wound closure and keeping the mesh flat in a tension-free manner.

Next, a discussion of dyspareunia and vaginal pain is undertaken in the monograph. The monograph notes that the dyspareunia rates can be as high as 9%. Dyspareunia may resolve with time with local treatment. Intervention is required in only a small fraction of patients. The monograph is clear that this may be related in part to surgeon experience and technique. Surgeons need to explore the state of the patient's pelvic floor musculature before surgery. Pre-existing pelvic floor dysfunction may explain clusters of patients with fibromyalgia and pelvic pain who develop postoperative dyspareunia. Patients more affected by dyspareunia include the elderly sexually active patient. Thus, it is important to carefully select patients who will be considered for the Prolift procedure. Defacatory dysfunction with or without tenesmus has also been noted. The monograph describes that the most important suggestion for prevention of this

complication is to strictly adhere to tension-free principles. Rectal exam at the conclusion of the procedure is the best assessment of this tension in the posterior compartment.

Finally, the monograph discusses a clinical data summary from approximately 550 patients followed for a mean of 6 months. Complications noted include rectal injury, bleeding, retention, and bladder injury. Mesh exposure was noted in 6.2% of patients. Sexual limitation occurred in 5-8% of patients.

Prolift is relatively safe for its intended use in treating symptomatic POP:

The surgical passage of Prolift canulae is relatively safe. Surgeons are familiar with the anterior passage of Prolift as many had been performing transobturator slings which traverse the same path as the anterior Prolift. Surgeons were performing similar posterior repairs using instruments such as the Capio device to reach the sacrospinous ligament. Similarly, surgeons are able to visualize the trocar passage of the Prolift procedure through tactile feel and visualizing the sacrospinous ligament using appropriate retractors. This is similar to how surgeons pass various needles, and trocars for abdominal procedures, SUI procedures, and pelvic floor repair procedures. When performing sacrospinous ligament fixation and other such procedures where the surgeon cannot easily visualize where the sutures are going, there is risk for significant complications. These can include: hemorrhage, pudendal nerve injury, rectal or bladder injury, and recurrent anterior vaginal wall prolapse. The trocar passage is not a blind passage of the trocar. When placing the trocar with the guide, the surgeon's finger should be positioned in the paravaginal space against the obturator internus muscle near the

pubic arch in order to meet the instrument. In this manner, there is very little tissue between the trocar and the surgeon's finger allowing for safe passage. This enhanced tactile ability in a well dissected surgical field with excellent assistance from hydrodissection and a thorough understanding of pelvic floor anatomy makes this procedure safe to perform with minimal morbidity. It is well-known that in any pelvic floor surgery that the surgeon should consider cystoscopy to check the integrity of the bladder, urethra and ureters. This information is obvious to all surgeons performing pelvic floor surgery. Core textbooks in Urology such as Campbells Urology (1998) discuss bladder injury in detail. A lengthy section within Chapter 32 discusses the potential complications of vaginal surgery. The section highlights that the vast majority of complications are preventable when the operator is aware of the hazards and risk factors in any given patient based on her postoperative history, physical examination, and preoperative tests. It further mentions that early recognition and appropriate intervention can minimize any sequelae.

For example, bladder injury is discussed in great detail:

- **Bladder Injury:** This complication can result from misplaced or deep operative incisions over the anterior vaginal wall, misplaced sutures, perforation during suture transfer, excessive electrocautery, or extreme medial displacement of the scissors when entering the retropubic space. Campbells Urology (1998) discussed the importance of intraoperative cystoscopy as well as strategies for how to deal with such an injury. Further, the discussion of delayed recognition of suture material is mentioned. The importance of recognizing that postoperative irritative voiding symptoms as persistent UTI

must be recognized. If the sutures are found, these can be removed with endoscopic scissors.

It should be obvious to any surgeon operating in the posterior pelvic floor that a rectal injury is possible whether mesh is used or not. Careful DRE should be performed in all such cases because of the anatomical proximity to the rectum. In fact, many surgeons will perform posterior repairs with a gloved finger in the rectum or Hegar dilator to help them recognize this structure. This is inherent to any pelvic floor surgeon who performs POP surgery.

It is well accepted that postoperative voiding dysfunction can occur after any pelvic floor surgery. This risk should be known by all surgeons who perform POP procedures. This does not need to be mentioned by Ethicon in the IFU. This information is well described in Campbells Urology (1998) Chapter 32, "Vaginal Reconstructive Surgery for Incontinence and Prolapse" Infection: The infection of sutures and other permanent graft materials can result from vaginal contamination and should occur in less than 1% of patients. Pain is a common complaint. Lower urinary tract infections are common in the first month after vaginal surgery and often respond to a short course of antibiotics. However, persistent UTI may be the presenting complaint when erosion of suture and bolster materials occurs in the urinary tract. This can cause delayed symptoms occurring months to years later.

Another way of looking at restoring vaginal anatomy is to look at the anatomical recurrence. Ow (2016) sought to assess anatomical outcomes in native tissue (NT) and transvaginal mesh (TVM) repair in women with recurrent prolapse. Of 336 repairs, 196 were performed in the anterior compartment and 140 in the posterior compartment.

Compared with the TVM groups, women undergoing repeat NT repair were more likely to experience anatomical recurrence (anterior 40.9% vs 25%, p = 0.02, posterior 25.3% vs 7.5%, p = 0.01), report vaginal bulge (anterior 34.1% vs 12%, p < 0.01, posterior 24.1% vs 7.5%, p 0.02) and had a higher prolapse re-operation rate (anterior 23.9% vs 7.4%, p < 0.01, posterior 19.5% vs 7.5%, p = 0.08). Using composite outcomes, the success rate was higher with TVM repair in both compartments (anterior 34.2% vs 13.6%, p <0.01, posterior 56.6% vs 23.0%, p <0.01). Re-operations for mesh exposure were 9.3% anteriorly and 15.1% posteriorly. Although the number of women requiring a prolapse re-operation is lower in the TVM group, the overall re-operation rate was not significantly different when procedures to correct mesh complications were included. The authors concluded that although the success rate is better with the use of TVM for recurrent prolapse, the total re-operation rates are similar when mesh complication-related surgeries are included.

Chronic pelvic pain can be a result of any pelvic floor surgery whether mesh is used or not mesh. This is a risk that is commonly known to pelvic floor surgeons. Of note is the posterior pass of the Prolift needle during the posterior compartment (rectocele) repair only passes through the ischiorectal fossa and then directly through the sacrospinous ligament. This is easy to feel and easy to perform. In my experience with Prolift, no patient has ever complained to be about chronic pelvic or buttock pain. Further, Campbells Urology (1998) described these issues well before Prolift was available in Chapter 32: Vaginal Reconstructive Surgery. For the Raz suspension, the authors note several short-term complications (including vaginal spotting, urinary tract infections, and irritative symptoms) and long-term complications (including de novo urge

incontinence, enterocele, prolonged voiding dysfunction and suprapubic pain). The text also discusses potential complications for the Gittes procedure, including urinary retention, suprapubic pain or cellulitis, vaginitis, suture infection (with abscess formation), and genitofemoral nerve entrapment.

As stated in the Ethicon patient brochures, IFUs, and Professional Education materials, mesh erosion extrusion and contraction can occur all of these can be associated with postoperative pelvic pain and thus dyspareunia. In addition, the importance of vaginal wall sensation and vaginal vasocongestion (ability to form a transudate) is important to promote healthy sexual activity. Weber (2014) evaluated the effects of vaginal mesh surgery on vaginal vasocongestion and vaginal wall sensibility in patients with recurrent POP. Vaginal wall sensibility and vasocongestion would be important sexual parameters to evaluate in patients undergoing a surgical procedure for POP. To this effect, 16 women were included, 14 completed the 6-month follow-up visit. Vaginal vasocongestion under erotic conditions did not significantly alter after mesh implantation. Vaginal wall sensibility of the distal posterior wall was significantly increased after mesh surgery (preoperative threshold 6.3 mA vs. postoperative 3.4 mA, $P = 0.03$). Sexual function as assessed with questionnaires was not significantly affected. The authors concluded that in women with a history of vaginal prolapse surgery, vaginal mesh surgery did not decrease vaginal vasocongestion or vaginal wall sensibility. Vaginal vasocongestion prior to mesh surgery appeared to be lower than that of women never operated on. Apparently, native tissue repair decreased preoperative vaginal vasocongestion levels to such extent that subsequent mesh surgery had no additional detrimental effect.

It is true for all POP surgeries performed that the complications that are known in terms of the incidence is not truly known, but is best described by the medical literature at any given time. This is because we must rely on published materials, which may underreport or not report at all their complications with POP surgeries. Also, there are no reporting mechanisms in place for complications that occur with native tissue repairs, so there is significant under-reporting of native tissue complications. Kasyan (2014) evaluated the rates of complications of pelvic organ prolapse repair and to determine their risk factors. 677 patients operated for POP with trocar guided Prolift mesh. Patients were followed up within 1 and 3 months. A phone interview was conducted and patients with complaints were invited and evaluated in office settings. Mean age was 60 years. For the phone interview, 86.5% of patients were available. Overall complication rates were 22.5% (152/677). Fifteen patients (2.2%) developed bleeding over 500 cc; pelvic hematomas - 5.5%; perineal hematomas - 2.5%; urethral injuries - 0.3%; bladder injury in 1.6%; rectal damage in 0.7% and ureteral trauma in 0.2%. Mesh related complications included: erosions in 4.8%; vaginal synechiae - 0.3%; protrusion of mesh into the bladder - 0.15%; vesicovaginal fistula with mesh protrusion - 0.3%; mesh shrinkage - 1%; dyspareunia and pain in 2.4% cases. Pelvic abscess was found in 0.6% including one case of lethal necrotizing fasciitis. The risk factors of complications were assessed via logistic regression analysis. The authors concluded that younger age, less prominent prolapse, hematomas and concomitant hysterectomies are associated with higher risk of complications.

Gad (2013) undertook a retrospective case analysis of the outcomes of 41 Prolift mesh repairs performed on 40 women over a 5-year period by a single surgeon in a

private hospital in Australia. They found successful anatomical correction and bulge symptom resolution were observed in 100% (2/2), 91.6% (11/12) and 100% (27/27) of anterior, posterior and total Prolift, respectively. Prolapse in a non-treated compartment occurred in one woman. Two patients developed postoperative hematomas requiring surgical evacuation; one of whom developed urinary retention for 2 weeks. Preoperative urinary symptoms were reported in 35/40 (92%) of women, 8 of whom reported only urge symptoms and experienced complete resolution after Prolift. Resolution of SUI in women who had urodynamic stress incontinence with and without urge symptoms was reported in 60% (12/20) and 20% (1/5), respectively. This represented 62.5% (10/16) and 33.3% (3/9) of women who had total Prolift and posterior Prolift respectively. Average follow-up periods were 7 and 39 weeks in 38 and 18 women, respectively. Gad concluded that the Prolift procedure is safe and effective in women with severe POP with resolution of most of the bulge and urinary urge symptoms. Total Prolift was effective in the treatment of associated mixed urinary incontinence.

It is well-known that slings can be placed at the time of POP repair in a patient with occult stress incontinence that is discovered at the time of urodynamics. If a sling is not placed in such patients 65% will ultimately need a sling placed at another time. Therefore, in a patient with occult stress incontinence, placement of a sling procedure at the same time a prolapse repair is considered appropriate and efficacious. van der Ploeg (2015) evaluated vaginal prolapse repair combined with midurethral sling (MUS) versus prolapse repair only. Women were randomly assigned to undergo vaginal prolapse repair with or without MUS. Analysis was according to intention to treat. The primary outcome at 12 months' follow-up was the absence of urinary incontinence (UI) assessed with the

UDI and treatment for SUI or overactive bladder. Secondary outcomes included complications. 134 women were analyzed at 12 months' follow-up (63 in MUS and 71 in control group). More women in the MUS group reported the absence of UI and SUI; respectively 62% versus 30% UI (relative risk [RR] 2.09; 95% confidence interval [CI] 1.39-3.15) and 78% versus 39% SUI (RR 1.97; 95% CI 1.44-2.71). Fewer women underwent treatment for postoperative SUI in the MUS group (10% versus 37%; RR 0.26; 95% CI 0.11-0.59). In the control group, 12 women (17%) underwent MUS after prolapse surgery versus none in the MUS group. Severe complications were more common in the MUS group, but the difference was not statistically significant (16% versus 6%; RR 2.82; 95% CI 0.93-8.54). The authors concluded that women with prolapse and co-existing SUI are less likely to have SUI after transvaginal prolapse repair with MUS compared with prolapse repair only.

Lowman (2016) evaluated the risk of serious adverse events with transvaginal mesh in an abstract presented at the American Urogynecology Society Meeting. They undertook a systematic review of the literature published from 2005 to 2016 and calculated the rate of serious adverse events. They noted that the risk of mesh infection requiring surgery for transvaginal mesh procedures was 0.2% and the risk of mesh contraction was 0.4%. Visceral injury occurred in 1.1% of patients and fistula in 0.2% of patients. These risks, when compared to traditional repair procedures and abdominal sacrocolpopexy were notably less. The authors concluded that the risks of serious adverse events with transvaginal mesh surgery are comparable to serious adverse events with other surgical procedures commonly performed to treat POP.

Lack of Scientific Data to Support Claims of Carcinogenic Potential of Pelvic Mesh

The host response to implanted materials of synthetic origin has been well studied in animals. Similar such studies have been undertaken in humans over the last few years. Moalli (2014) reviewed the potential for carcinogenicity with polypropylene mesh in their review article. The authors noted that potential for neoplasm from such implanted mesh has never been shown to be causative. They cited an epidemiologic study by the International Agency for Research on Cancer (2000) that concluded that there was no evidence for tumorigenicity of metallic or synthetic implants in humans. The authors propose that the potential for carcinogenesis of polypropylene mesh is negligible when the low incidence of reports of carcinogenesis is considered given the world wide use of polypropylene as a suture for hernia mesh in millions of patients over the last 50 years. Finally, the authors state the similarity of mesh to the use of breast implants in that millions of women have been treated successfully with no evidence of systemic complications including cancer and haven been able to have significant improvement in their quality of life as a result of their surgery.

Linder (2016) evaluated the carcinogenic potential of implanted synthetic mesh midurethral slings for SUI. They identified 2474 patients who underwent SUI surgery with a midurethral sling. With a medial follow up of 60 months, only 2 cancers (0.08%) developed following sling placement. Neither of these tumors had any relationship to the sling placement. Both tumors were of gynecologic origin (vaginal melanoma and ovarian tumor). There were no cases of sarcoma, bladder or urethral or squamous cell carcinoma identified. They concluded that with a medial follow up of 5 years after synthetic midurethral sling that the development of pelvic malignancy is rare (0.08%) and is unlikely to be related to foreign body reaction from the implanted material.

Adel (2016) reviewed the carcinogenic potential of polypropylene mid-urethral slings. The authors searched multiple online databases for information related to any possible carcinogenic potential of polypropylene mesh. They concluded that the likelihood that the mesh causing malignancy is exceptionally low. To date, there is no reliable scientific data suggesting a link between Ethicon's polypropylene meshes and cancer.

Lack of Scientific Evidence to Support Claims of In Vivo Mesh Degradation

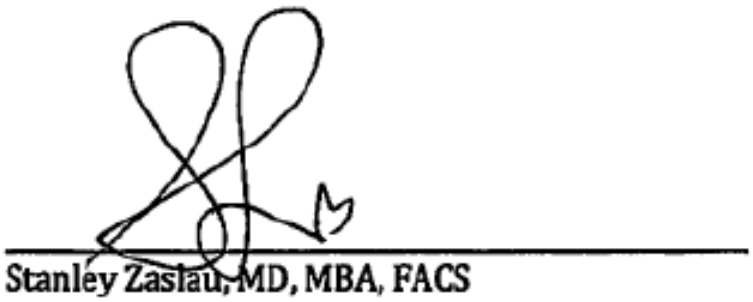
Plaintiffs' experts in the MDL cases allege that polypropylene mesh undergoes degradation. These claims are without scientific validity and are not considered reliable or generally accepted in the medical community. There are no reliable clinical studies demonstrating any clinical significance associated with alleged degradation. There are also, over the last year, several studies have been published or presented that suggest that mesh does not degrade. For example, Ong (2016) presented an abstract at the International Urogynecological Association Meeting on the morphology and material chemistry of explanted Prolene meshes with a novel cleaning process that does not utilize formalin. With electron microscopy, they showed that the Prolene mesh did not undergo meaningful or harmful degradation in vivo. They found that there was a cracked layer over the Prolene fibers that was related to adsorption of the formalin fixative used in preparation of the explanted specimens.

Following up on their abstract, Thames (2016) was concerned with the cleaning protocol utilized to analyze mesh that has been removed from patients. They sought to create a nondestructive, hydrophilic cleaning process and utilize microscopy and spectroscopy of the specimens. 78 explanted Prolene meshes were analyzed that were

implanted between 0.4 and 11.7 years. They concluded that their cleaning process of explanted Prolene meshes showed that they did not degrade in vivo. This confirms the decades of excellent clinical results, in vivo stability, and biocompatibility of Prolene within the body. The authors further concluded that the cracked layer previously suggested to be degraded Prolene was actually due to adsorbed protein-formaldehyde coating from formalin fixation. This confirms similar findings of other authors who found no polymer degradation after cleaning the biofilm from the explants. (DeTayrac 2011).

CONCLUSION:

In conclusion, my clinical experience and ongoing analysis of the medical literature supports my opinion that Gynemesh PS and Prolift are safe and effective for the transvaginal treatment of pelvic organ prolapse, that the benefits of Gynemesh PS and Prolift outweigh the risks; that the Gynemesh PS mesh used in Prolift was appropriately designed for its intended use and is not defective; that Gynemesh PS and Prolift are not defective simply because there is a potential for a patient to experience a commonly known complication; and that the complications associated with the Prolift procedure are commonly known to occur with any pelvic floor repair procedure.



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